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THE CLINICAL AND ROENTGENOLOGIC MANIFESTATIONS AND SURGICAL TREATMENT OF DIAPHRAGMATIC HERNIA, WITH A REVIEW OF 131 CASES[1]

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IT is gratifying to have the opportunity to present the subject of the diagnosis and surgical treatment of diaphragmatic hernia before this Congress because roentgenography plays an important rôle in the recognition and differential diagnosis of diaphragmatic hernia. It is also of great value in determining the size and situation of the defect in the diaphragm, which is of aid in determining the method of surgical treatment to be instituted.

The incidence of diaphragmatic hernia is probably no greater now than it was twenty years ago; at that time the condition was thought to be uncommon, and its recognition in life was rare. More frequent recognition of the condition in the last two decades has been attributable primarily to development of roentgenologic methods of diagnosis. The clinical study of proved cases has established a fairly definite symptomatology which has enabled the clinician to diagnose the condition or to suspect the presence of a hernia and to have a special roentgenologic examination made. It will scarcely be claimed that the entire credit for the present more frequent recognition of this condition is due the roentgenologist, but he is entitled to share this credit with the clinician. A greater proportion of the responsibility for the establishment of the correct diagnosis must rest on the clinician, for he is first to come in contact with the patient, and the subsequent course of the examination and treatment depends on his interpretation of symptoms.

The more frequent recognition of diaphragmatic hernias in recent years is exemplified by reviewing the cases encountered at The Mayo Clinic between 1900 and 1937. From 1900 to 1925, 30 cases were recognized clinically and 19 patients were operated on; from 1925 to 1937, 211 cases were recognized and 131 patients were operated on. This shows that seven times as many cases were recognized in the last 12 years as in the previous 24 years. We believe that the condition is more common than the present records indicate, for one of us (S. W. H.) has examined the diaphragm in the course of other abdominal operations and occasionally has found a small hernia that had not been recognized clinically or roentgenologically before operation.

CLASSIFICATION

Because of the various structures which are often involved in the hernia the symptoms are complex. They depend on the amount of mechanical interference with

[1] Read by Dr. Harrington before the Fifth International Congress of Radiology, Chicago, Sept. 13–17, 1937.

the hernia is usually para-esophageal. In the second class, the intestines, with or without involvement of the stomach and other abdominal viscera, are included in the hernia. In these cases the hernia usually is of traumatic origin and thus of the acquired type, but may be of congenital origin, in which there is a structural deficiency of the diaphragm.

Para-esophageal diaphragmatic hernia may be considered to be of the non-traumatic congenital or acquired type or it may be considered, in some cases, to be traumatic, but it is essentially congenital. There may be a congenital weakness of the esophageal ring, and a definite hernia may later be produced by some type of injury or by increased intra-abdominal pressure. Recently one of us (S. W. H.) reviewed the results of examination in 1,000 cases in which the esophageal hiatus was examined in the course of other abdominal operations, and in 55 per cent of cases the esophageal ring was closely approximated to the esophagus by loose areolar tissue and there was no appreciable space between the two structures. In 35 per cent of cases at least one finger, or more than one, could be placed between the esophagus and the margin of the esophageal ring. In 8 per cent of the cases two fingers, and in 2 per cent three fingers could be placed between the esophagus and the margin of the opening. When one or two fingers can be inserted between the esophagus and the esophageal ring, the diameter of the hiatus may be considered to be within normal limits. In those cases in which three fingers could be inserted through the opening, special roentgenograms were made subsequently, and in two of these cases a small hernia was found. It is improbable that in all cases in which the esophageal hiatus is enlarged, hernias will ultimately develop, but hernias may develop later if the intra-abdominal pressure is sufficiently increased. Such increase in pressure may be caused by an injury or by any other condition which increases intra-abdominal pressure, such as obesity, pregnancy, severe strain or exertion such as is produced during vomiting or by violent physical exercise. Hernias following such causes may be considered of traumatic origin but they are essentially congenital, in the same manner that hernias in the inguinal region are congenital.

Para-esophageal hernia is the most common kind of hernia through the diaphragm that is found in adults. It is a true hernia, for a hernial sac is formed of diaphragmatic peritoneum, which fuses with the serosa of the stomach. In most instances this hernial sac is attached to the cardiac end of the stomach, at varying distances from the cardia, which suggests that this kind of hernia is produced by closure of the diaphragm around the stomach before the esophagus has elongated sufficiently to permit the stomach to reach its normal position below the diaphragm, thus producing a large esophageal hiatus. Later the stomach descends to its normal position below the diaphragm and herniates through this enlarged esophageal hiatus. Para-esophageal hernias are slowly progressive and constitute a sliding herniation of the stomach into the posterior mediastinum; they may push into either or both thoracic cavities but do not enter the pleural cavity. The stomach is usually the only abdominal viscus involved in the hernia. These hernias may progress until the entire stomach is contained within the hernial sac, and in these extensive cases the colon and omentum may also be drawn into the sac.

The symptoms of para-esophageal hernia may begin at birth or at any time in life. This kind of hernia produces more uniform symptoms than hernias elsewhere in the diaphragm. The symptoms are those of intermittent, and usually progressive, incarceration and obstruction of the stomach. At the onset, the attacks are usually mild; they consist of epigastric distress that is projected through to the back and comes on in the course of, or shortly after, a heavy meal; but they may be brought on by taking anything into an empty stomach, such as a cupful of coffee. The attacks are usually similar in character but vary a great deal in intensity, depending on the amount of incarceration and fixation of the stomach

in the hernial opening. They are usually relieved by belching of gas and vomiting and are commonly considered to be attributable to cholecystitis, for which the patient is usually treated. As more of the stomach becomes incorporated in the hernia, the attacks become more severe; the pain is projected straight through to the back and to the lower left side of the thorax, is more marked to the left of the spinal column and often appears between the shoulder blades. This pain may be agonizing, and there is difficulty in belching of gas and vomiting because of spasm of the diaphragm and reflex cardiospasm. The spasm of the diaphragm produces an hourglass deformity of the stomach, which interferes with emptying of the upper loculus and causes increased intragastric pressure. The pressure of the herniated portion of the stomach on the lower part of the esophagus interferes with belching of gas or vomiting.

Spasm of the diaphragm is commonly associated with phrenic pain which is referred to the left shoulder and which at times may extend down the left arm. The increased pressure within the thorax causes cardiac embarrassment, with palpitation and tachycardia. Pressure on the lung and interference with the motion of the diaphragm cause dyspnea. These symptoms are augmented when the patient lies down, and in the more severe cases it is necessary for patients to sit up to breathe. The attacks may last for from a few minutes to several hours, and not uncommonly are considered to be caused by myocardial disease, relative to which the most frequent diagnosis is that of angina pectoris. The attacks often recur immediately after food has been taken. There is often an interval of weeks or months between attacks. It is probable that during the interval between attacks the stomach is not incorporated in the hernial ring and is in its normal position below the diaphragm. When the attacks become more or less constant, the stomach usually has become fixed in the thorax by adhesions. All the early symptoms of pressure are augmented during attacks. There is loss of weight from inability to retain food and from marked restriction in diet because of the fear of bringing on an acute attack of gastric obstruction. This may be termed "food-fear."

The vomiting is more severe during attacks and often is of the retention type. During the severe vomiting the vomitus may contain blood. If the attacks are of long standing, the patient not uncommonly has a burning sensation in the epigastrium after meals, which is relieved by taking small quantities of food. If a large amount of food is taken it may bring on one of the attacks associated with incarceration of the stomach. Many of these patients present a fairly good syndrome of ulcer, are given medical care, and obtain partial relief because they have taken a restricted amount of food at frequent intervals.

Hemorrhage is not a common symptom; it usually is indicative of severe incarceration, with fixation of the stomach in the thorax. The bleeding is caused by erosion or ulceration of the mucous membrane, resulting from the forceful pressure exerted during the attacks of vomiting on the large, distorted and congested stomach and to the trauma caused by the hernial ring as the stomach is forced in and out of the opening. This erosion may be superficial, or, in cases of long-standing, definite ulceration may form from repeated trauma. This is usually the final stage of incarceration. Strangulation of the stomach as a result of hernia has not been observed at the clinic and it is to be doubted that strangulation is possible because of the powerful musculature and rich blood supply of the gastric wall. Because of the fixation of the stomach in the thorax, the obstruction may be complete, and the vomiting may be so severe as to produce gastric tetany.

Patients who have para-esophageal hernia, of which the predominating symptoms are those of esophageal obstruction, are of particular interest and require careful clinical study. The symptoms may be attributable to an entirely unassociated lesion of the lower part of the esophagus, such as cardiospasm, carcinoma, or diverticulum,

or they may be the result of ulceration or stricture of the esophagus caused by the hernia. This esophageal ulceration produced by the hernia is attributable to the repeated or constant pressure of the hernial sac on the lower part of the esophagus or to the regurgitation of food or gastric secretion into the lower part of the esophagus. The ulceration may be a small localized lesion or it may involve the entire circumference of the lower part of the esophagus and later may contract and produce a stricture. Because of the possibility of there being a lesion in the lower end of the esophagus caused by or unassociated with the hernia, we believe an esophagoscopic examination is advisable in all cases.

The foregoing is the clinical picture in a typical case of slowly progressive herniation of the stomach through the esophageal hiatus, but, of course, it cannot be expected that every case will present all the symptoms, any more than it can be expected that a typical history will be elicited in every case of any other organic condition. The chief symptoms depend, to some extent, on the time in the course of the disease at which the patient is examined, on the rapidity with which the hernia has been produced, on the amount of fixation of stomach in the thorax, and on the amount of disturbed function of thoracic organs.

The symptoms of traumatic hernia or of non-traumatic, congenital types of hernia in which the stomach only is involved in the hernia, are essentially the same as those described but are usually more severe and acute and do not extend over as long a period. Cases of this sort are relatively rare, because in these types of hernia usually the large and small bowel, as well as the stomach, spleen, and occasionally the liver, are involved in the hernia. There is no limiting sac and the herniated abdominal viscera are in direct contact with the lung and pericardium. The condition in these cases may be more properly termed "evisceration of the abdominal organs into the pleural cavity" rather than a "true hernia."

The symptoms in traumatic cases are very rapid in progress and severe in character, and are attributable to the mechanical interference with function of the herniated viscera as well as to marked interference with function of the heart and lungs. The symptoms in these cases are even more severe than those in congenital types of hernia because of the sudden alteration of the intrathoracic pressure as well as the mechanical interference with the function of the organs involved. The most marked immediate symptoms are usually those of respiratory and circulatory embarrassment. Later, severe hemorrhage from the gastro-intestinal tract may occur as a result of incarceration or strangulation of the hollow viscera. If the patient survives the acute condition, the later symptoms depend on the viscera involved. The symptoms may be those of obstinate constipation, the occurrence of large quantities of gas in the colon, and attacks of partial or complete intestinal or gastric obstruction. The sudden onset of symptoms in traumatic cases usually is related directly to the injury and there is rarely any question as to the clinical diagnosis. Surgical treatment is demanded because of the danger of cardiac and respiratory failure or of intestinal strangulation.

SURGICAL TREATMENT

The only treatment of diaphragmatic hernia which will prevent the occurrence of serious complications and assure relief of symptoms is the operative replacement of the herniated abdominal viscera and the repair of the abnormal opening in the diaphragm.

The methods and technic of the surgical procedures utilized in surgical treatment depend on the type, situation, and size of the defect in the structure of the diaphragmatic muscle, the kind and amount of abdominal viscera involved in the hernia, and whether or not the viscera are enclosed in the hernial sac. Details in the surgical treatment of all types of diaphragmatic hernia will not be entered into but general

surgical methods and some of the special technical considerations which are required in some types of hernia will be discussed.

There is only one type of diaphragmatic hernia that may be treated conservatively and that is hernia through the esophageal hiatus, when only a small portion of the cardiac end of the stomach is involved in the hernia and then only when the symptoms are mild. If symptoms become progressively more severe, the possibility of serious complications is great, and treatment in all such cases should be surgical, unless radical operation is contra-indicated because of the patient's general condition. Operation should be performed before severe incarceration, with consequent obstruction and traumatic lesions of the stomach, have occurred. The operative risk is increased by gastric retention, and the technical difficulties are enhanced by fixation of the stomach to the diaphragm and to the hernial sac within the thorax.

All cases in which the colon or small bowel are involved in the hernia demand early operation because of the danger of intestinal obstruction. However, these cases are usually traumatic in origin and it is best not to operate until the acute symptoms caused by the primary injury have subsided if the patient's condition will permit.

Interruption of Phrenic Nerve.—Paralysis of the diaphragm, produced either by temporary or permanent interruption of the phrenic nerve, is of value as a procedure preliminary to radical operative repair of many different types of diaphragmatic hernia. It is a necessary procedure in the surgical treatment of partial thoracic stomach resulting from a congenitally short esophagus. In some cases in which radical operative repair is contra-indicated it may be used as a palliative measure. In most instances interruption of the phrenic nerve is utilized as a procedure preliminary to radical operative repair of the hernia.

RADICAL SURGICAL REPAIR

Anesthesia.—Ethylene or cyclopropane is preferable as the anesthetic agent, and the method of administration depends on the type of hernia which is present. In all cases in which there is no hernial sac and n which there is a direct communication between the abdominal and thoracic cavities, intratracheal administration of the anesthetic agent by means of a positive pressure machine is preferable. In cases in which there is a hernial sac, as in the para-esophageal type of hernia, the anesthetic agent can be administered by the closed-mask method.

General Technical Considerations.—Both the abdominal and the thoracic approach in reduction and repair of these hernias have been employed. In two cases in which the thoracic approach was used it was necessary to resort to a combined thoracic and abdominal procedure in order to free the adherent abdominal viscera from the abdominal side of the diaphragm, if repair was to be accomplished without injury to abdominal viscera. In one of these cases post-operative empyema developed, necessitating drainage and resection of a rib before ultimate recovery could take place.

In treatment of all hernias through the left hemidiaphragm, the abdominal approach through an oblique left rectus incision is preferable, starting at the ensiform cartilage and extending to the outer border of the rectus muscle. There is less risk of thoracic complications when this approach is used. It is of particular advantage in cases of esophageal hernia, for the herniated stomach is usually confined in a sac in the posterior mediastinum and does not enter the true pleural cavity.

In hernias through the right hemidiaphragm, the thoracic approach is chosen because the large, right lobe of the liver makes the abnormal opening in the diaphragm inaccessible from the abdominal approach.

The technical difficulties of adequate exposure of the hernial openings through the left hemidiaphragm and the esophageal hiatus are often considerable because of fixation of the left lobe of the liver to the leaf of the diaphragm. The exposure of

these hernial openings is greatly facilitated by cutting the suspensory ligament and retracting the left lobe of the liver to the right. This can be accomplished, when the left lobe is small, by folding it on itself, and when it is large, by retracting it forward into the wound. The spleen is often very adherent to the posterior part of the diaphragm and hernial openings but usually can be separated from these structures by blunt dissection. It is retracted posteriorly by a properly constructed retractor. In some instances the spleen may be so traumatized by separating it from the hernial opening in the thoracic portion of the diaphragm that it is advisable to remove it. This occurred in two cases of this series.

Hernia through the Esophageal Hiatus.—Because para-esophageal hernia is the most common type seen in adults, this is the only special type of hernia in which the details of surgical treatment will be given here. These hernias through the esophageal hiatus have a hernial sac. The attachment of the sac to the stomach must be separated and the sac either completely removed or permitted to retract into the posterior mediastinum. This is one of the most important technical considerations in the surgical treatment of these hernias.

After the sac has been removed, the enlarged esophageal hiatus is repaired by overlapping the margins of the opening. Closure is usually made to the left of the esophagus, but in some cases it is necessary to close, partially, both to the right and left of the esophagus. In a few instances the enlargement of the esophageal opening is posterior, extending to the spinal column and requiring the overlapping of the margins posterior to the esophagus. In such cases the condition is often thought to be a herniation through the aortic opening, but usually extending over the aorta there is an imperfectly developed fibrous band which is the margin of the defective esophageal hiatus. The closure is usually made with living sutures of fascia lata which are removed from the thigh. The overlapped margins of the hernial opening are first stabilized with interrupted linen sutures. The fascia lata is then woven into the tissues by continuous suture and fixed in the tissues with interrupted linen sutures.

Before closure of the defective esophageal hiatus is completed around the lower part of the esophagus it is important that a stomach tube of large caliber be placed through the esophagus into the stomach to aid in the reconstruction of the normal esophageal opening and to prevent constriction of the esophagus by a tight closure. A small portion of the esophageal wall is incorporated in the innermost margin of the closure by a suture of chromic catgut.

Not uncommonly in these cases there is an associated traumatic erosion in the herniated portion of the stomach, along the lesser curvature, close to the cardia, and this erosion is often adherent to the margins of the hernial opening. Great care should be used in replacing the stomach in the abdomen and in removing the sac from the stomach because of the danger of perforating this thinned-out portion. In cases in which the ulcerated portion is penetrated, it should be repaired immediately with continuous catgut and linen sutures. Perforation occurred in two cases of this series, and the perforated portion was immediately repaired and the patients had an uneventful convalescence.

The abdomen should always be thoroughly explored for any other lesion, particularly of the stomach or gall bladder. In some cases it may be necessary to operate on other associated lesions, as occurred in two of this series. In one of these cases it was necessary to perform gastric resection because of a perforating ulcer high on the lesser curvature, which was probably secondary to a traumatic erosion; in the second case the patient had a large, obstructing duodenal ulcer for which it was necessary to perform gastro-enterostomy. It is inadvisable to carry out any additional surgical procedure at the time of repairing the hernia unless it is imperative, but it is well to know if the patient has gallstones or any other lesion in the upper part of the abdomen which might account for subsequent symptoms.

COMMENT ON THE OPERATIVE PROCEDURES EMPLOYED AND ON THE RESULTS IN THE 131 CASES

The operative procedures in the 131 cases on which this paper is based were as follows: In 64 cases the phrenic nerve was either temporarily or permanently interrupted preliminary to operative repair of the hernia. In eleven cases permanent interruption of the left phrenic nerve was done as a palliative measure or as a therapeutic test; in five of these cases, the hernias were para-esophageal and operation was contraindicated; in the remaining six cases, herniation of the stomach was attributable to a congenitally short esophagus for which the procedure was done as a therapeutic test. In these cases it may be necessary to do a radical operation later for complete relief of symptoms. In 120 cases the herniated abdominal viscera were replaced in the abdomen and the abnormal opening in the diaphragm was repaired. In two of these cases a combined thoracic and abdominal approach was employed; in the remaining 118 cases the abdominal approach was employed. In one case a Polya type of gastric resection was done at the time of operation for gastric ulcer high on the lesser curvature of the stomach. In one case posterior gastro-enterostomy was performed for a large duodenal ulcer which had caused almost complete obstruction of the pyloric end of the stomach. In two cases the spleen was firmly adherent to the margins of the opening and to the thoracic portion of the diaphragm; the spleen was torn during operation, which necessitated its removal. In one case, appendicostomy was performed at the time of operation because of marked dilatation of the colon which had resulted from partial obstruction during the time it was in the thoracic cavity. In ten cases there was moderate congenital shortening of the esophagus associated with the hernia; the diaphragm could be sutured entirely above the stomach after the diaphragmatic muscle had been paralyzed by phrenicotomy. In one case, extra-pleural thoracoplasty was performed preliminary to repair of the hernia. As noted in the first part of this paper, 21 of these patients had prior operations for the same complaint, without relief of symptoms, but were completely relieved following repair of the hernia.

There were seven deaths following operation; five of them occurred in cases of congenital hernia and two in cases of traumatic hernia. Four deaths occurred in the first 72 hours from respiratory and cardiac failure; three deaths occurred in the second week from pneumonia.

The results obtained in the 124 cases in which the patients recovered from the operation have been reviewed recently by one of us (S. W. H.). Of the eleven patients who were treated palliatively by interruption of the phrenic nerve, one has since died of angina pectoris; four, all of whom were more than seventy years of age, died of causes not definitely ascertained but which apparently were attributable to cardiac conditions, for the patients had myocardial degeneration at the time of the operations. The remaining six of these eleven patients have obtained partial relief of symptoms. One hundred thirteen patients recovered from radical operation for the repair of the hernia; 110 patients have been completely relieved of symptoms and three have had a return of symptoms following recurrence of the hernia. In one of the cases recurrence developed following an influenzal type of pneumonia, three months after operation; the recurrence was caused by the severe strain of coughing. In the other two cases there is no known cause for the recurrence. All patients have been examined roentgenologically every six months to a year after operation.

SUMMARY

The more frequent recognition of diaphragmatic hernia in recent years may be attributed entirely to the development of roentgenography. A study of proved instances of this condition has established symptoms and has enabled the clinician to suspect a diaphragmatic hernia; however, roentgenography is still the most impor-

tant factor in making a definite diagnosis. It is also of great aid in determining the size and situation of the opening and the type of abdominal viscera which has herniated. The symptoms are usually progressive and vary in type and intensity, depending on the amount and type of herniated abdominal viscera and the degree of mechanical interference with the normal function of the diaphragm, heart, and lungs. The symptoms often resemble those of other organic diseases of the abdomen and thorax, especially cholecystitis, peptic ulcer, cardiac disease, secondary anemia, and esophageal obstruction. Operative replacement of the herniated viscera and repair of the abnormal opening in the diaphragm is the only treatment that insures complete relief of symptoms. The hernial opening is best repaired through an abdominal approach, by using fascia lata and interrupted linen sutures. Temporary or permanent interruption of the phrenic nerve is of value as a preliminary procedure to radical closure of large openings, particularly when there is deficiency or loss of structure of the diaphragm.

The surgical procedures and results in 131 cases have been reported. Radical repair of the hernia was carried out in 120 cases. There were seven operative deaths. Of the 113 patients who recovered from radical operative repair of the hernia, 110 were relieved of symptoms. In the remaining three cases the hernia and symptoms recurred.

PELVIC ROENTGENOGRAPHY IN PREGNANCY[1]

FURTHER EXPERIMENTS WITH 90° TRIANGULATION METHODS

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THE most important roentgenologic contributions to obstetrics are nonquantitative, require little or no special apparatus, and call for only such experience and knowledge as are possessed by all qualified radiologists. Prominent examples of this group are:

(1) Diagnosis of pregnancy.
(2) Differentiation between single and multiple pregnancy.
(3) Diagnosis of fetal attitude, presentation, and position.
(4) Diagnosis of such perversions of pregnancy as ectopic pregnancy, missed abortion, hydatidiform mole.
(5) Demonstration of fetal deformities or disease.
(6) Estimation of amount of amniotic fluid and location of the placenta.
(7) Determination as to whether the fetus is alive or dead.
(8) Thoroughgoing qualitative survey of maternal pelvis.

Quantitative studies of the pelvis and fetus require somewhat specialized equipment and experience. One of us (P. C. H.) has recently discussed the general principles underlying all roentgen pelvimetry and fetometry (1) and most of the positions, equations, graphs, technics, classifications, and special apparatus mentioned in the present paper are illustrated and explained in that article.

OPTIMUM TIME FOR CONDUCTING EXAMINATION OF PELVIS

In cases in which economic conditions permit we recommend examination of the pelvis as soon as possible after the onset of pregnancy, followed by examination of the fetus *in utero* shortly before term. For the first part of this examination four, or at most six, films suffice, and for the second, two or four, depending on the particular technic employed. Even when one uses the maximum of ten films the amount of radiation absorbed by the skin of the mother is far below the erythema dose and that absorbed by the fetus is very small indeed. There is no reason at all to fear that this small amount of radiation will injure the fetus, and those who have expressed such fears presumably confuse the conditions of diagnostic raying with those of therapy.

The four to six pelvic films made early in pregnancy are distributed as follows:

(*A*) *Frontal Stereoroentgenograms* (*Position I*).—These are essential for general survey and classification but are not suitable for measurement of the inlet because of the obliquity of the view.

(*B*) *A Single Film or Stereoroentgenograms in the Lateral Position* (*Position II*).—From these one judges the shape and size of the sciatic notch, notes the vertical height of the pelvis, and measures the anteroposterior diameter of the inlet. This diameter as measured on the film is, of course, greater than the true anteroposterior diameter because of triangular distortion. If stereoroentgenograms have been made, distortion may be corrected with the aid of a measuring stereoscope or a stereoroentgenometer or by employing a correction factor obtained from a parallax graph. If but a single film is to be made, it is necessary to measure the distance from the midline of the body to the film at the time the examination is done. This measurement is the object-film distance (d) for those anatomical parts lying in the

[1] Presented before the Fifth International Congress of Radiology in Chicago, Sept. 13–17, 1937.

sagittal plane of the body. Laid off on a graph of Equation 1 (1) it supplies a correction factor for reducing distorted or gross anteroposterior diameter to net anteroposterior diameter.

(*C*) *A Single Film or Stereoroentgenograms Showing the Inlet* (*Position III*).—This view is superior to all others for qualitative study of the inlet as a whole and for measurement of its transverse diameter. If but a single film is used, the distance from inlet to film (d) must be measured at the time the examination is done. For such a single film or for stereoroentgenograms the work-up is the same as in case *B*, described above.

Some workers deliberately defer all examination until the closing weeks of pregnancy so that the study of the pelvis may be combined with that of the fetus. On the other hand, though the referring obstetrician may concur as to the desirability of early examination, exigencies may prevent this and require that one attempt pelvic measurements from films made late in pregnancy. The principal disadvantage lies in the fact that Position III, so essential to adequate study and measurement of the inlet, involves raying through the entire length of the enlarged uterus with resulting excessive scattering of radiation and blurring of film images.

EXAMINATION OF THE FETUS

The two or four fetal films that are regularly made late in pregnancy are distributed as follows:

(*D*) Two pairs of stereoroentgenograms, one pair in the frontal position (Position I), the other in the lateral position (Position II),

or

(*E*) One pair of 90° triangulation films, one in the frontal position (Position I), the other in the lateral position (Position II).

With either type of filming one proceeds first to the non-quantitative studies of the sort tabulated in the opening paragraphs of this paper, after which he measures various parts of the fetus and attempts to estimate its age. Usually such estimates are simply of academic interest, but they may assume clinical importance when the menstrual history is in doubt or the possibility of a dead fetus is being considered.

ESTIMATION OF FETAL AGE FROM OFD OR BPD

Theoretically it should be possible to measure occipitofrontal diameter with the aid of the measuring stereoscope or the stereoroentgenometer in every instance, regardless of the angular relationship between fetal skull and film. Practically such measurements are reliable only when the occipitofrontal axis lies in a plane approximately parallel with the plane of the film (Figs. 5-*a*, 5-*c*, and 5-*d*). The difficulty has nothing to do with the theory of stereoscopic triangulation, depending instead upon the fact that the so-called "end-points" of the occipitofrontal diameter do not constitute actual bony protuberances but are merely locations on the surfaces of flat bones.

When the occipitofrontal axis lies in a plane parallel with the plane of the film, the anterior and posterior poles of the skull appear as sharply silhouetted arcs. If there is any great degree of obliquity between axis and film, however, these poles do not appear in silhouette and identification of the end-points of the axis becomes difficult if not impossible (Figs. 5-*b* and 5-*e*). The situation is the same in the case of biparietal diameter, which dimension can be measured accurately only when the biparietal axis lies in a plane approximately parallel with the plane of the film.

It has been suggested by others (but not yet attempted by us) that when a preliminary examination demonstrates an oblique lie of both occipitofrontal and biparietal axes, an additional examination might be done after manipulation of the fetus or rotation of the mother under fluoroscopic control until one of these axes lies in a plane parallel with the plane of the film.

ESTIMATION OF FETAL AGE FROM AVERAGE CIRCUMFERENCE

Ball has hoped that his measurement of average right-angle circumference might indicate the true size of a fetal skull, regardless of its lie. We employ circumference with enthusiasm, believe we have demonstrated its fundamental soundness (1) and find it applicable in many cases where neither occipitofrontal diameter nor biparietal diameter can be measured, but we are convinced that this measurement like the others has its limitations (Figs. 5-*d* and 5-*e*).

Further stages in the development of a jacket method of 90° triangulation published by one of us (1) and additional experiments testing the usefulness of skull circumference as a guide to fetal size are dealt with in the material that follows.

Our original jacket, made of celluloid-impregnated stockinet stretched over a frame of aluminum tubing, was expensive to build and gradually pulled out of shape.

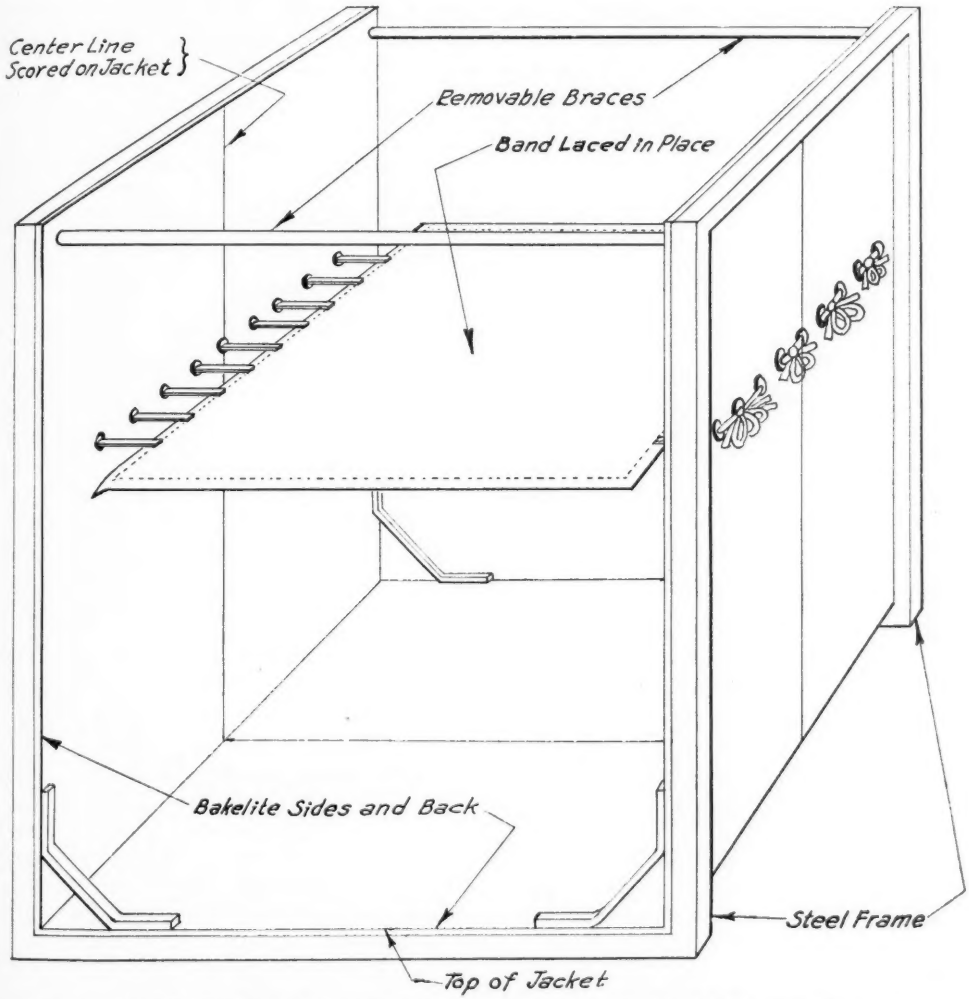

Fig. 1. Jacket for 90° triangulation. The original jacket was described in detail in an earlier article (1), and the modified jacket illustrated above is described in the text of the present article.

The present jacket (Fig. 1), made of sheet bakelite riveted to a frame of welded square steel tubing, is provided with cross-braces that are easily inserted after the patient is in place. These prevent bending of the sides of the jacket as the binder is tightened.

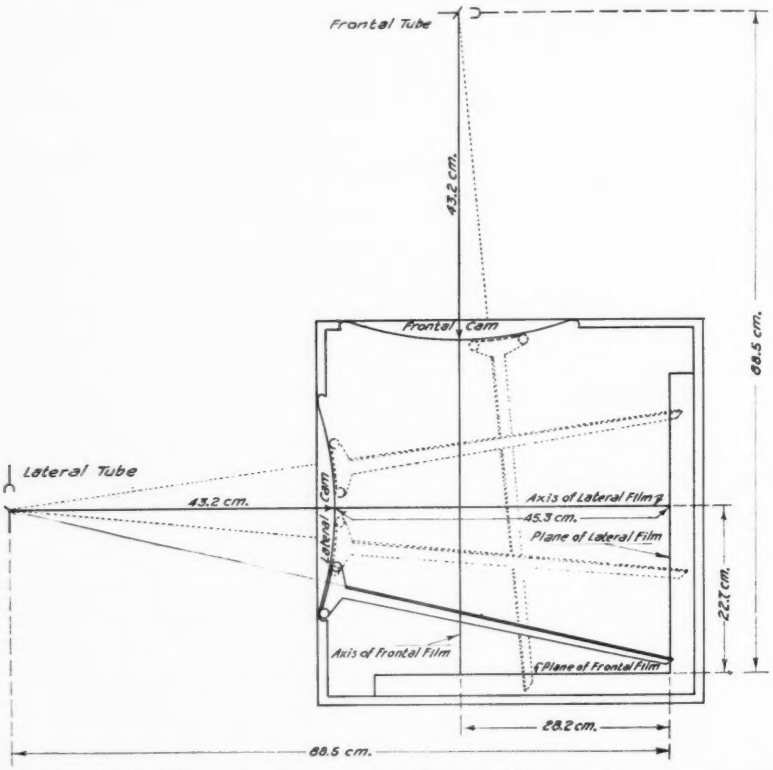

Fig. 2. Straight edge travelling on cam to indicate direction of radiation. Where space is available one needs merely a large drawing board with threads attached to two pins representing the targets of the two tubes and two metric rulers representing the planes of the two films. Such an apparatus is, in effect, McKenzie Davidson's cross-thread apparatus designed for two-dimension rather than three-dimension construction. It is clumsy to use threads pivoted 88.5 cm. out in space and more convenient to use cams curved and located so that straight edges moving along their surfaces correspond to threads stretched from pivots 88.5 cm. distant.

TRAVELLING STRAIGHT-EDGE INSTRUMENT FOR WORKING UP 90° TRIANGULATION FILMS

For the work-up of 90° triangulation films we no longer employ plotting charts but instead an instrument composed of travelling straight edges and scales which, for economy of office space, has been incorporated with the bed of our stereoroentgenometer without interfering with the use of the stereoroentgenometer for other purposes (Figs. 2, 3, 4). By means of this instrument computations of all sorts are eliminated and one obtains by graphic means alone correction factors for skull circumferences and diameters in both films. Like all detailed descriptions of geometric instruments, a description of this one will at first seem rather complicated. Anyone who has studied high school geometry and algebra will find, however, that both the instrument and its application are quite simple once the newness has worn off. It must be admitted that the average roentgenologist will probably need the assistance of a machinist, physicist, engineer, or mathematician while

he is setting up an instrument designed to meet the conditions of his particular laboratory, but once this has been done he can other workers. It is important merely that the values be known and that in the instrument used for working up films they

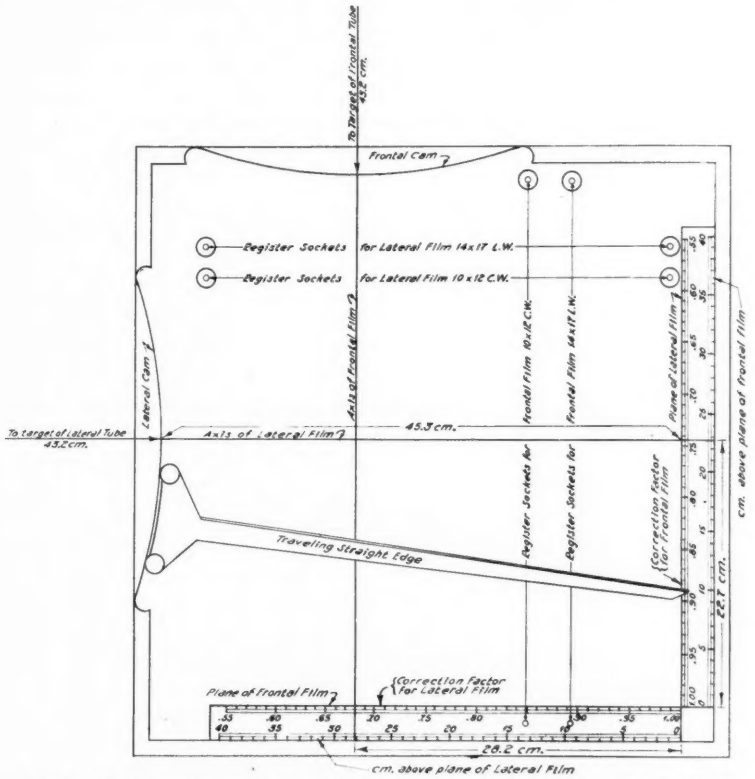
To Target of Frontal Tube 43.2 cm.
Frontal Cam
Register Sockets for Lateral Film 14x17 L.W.
Register Sockets for Lateral Film 10x12 C.W.
Axis of Frontal Film
Frontal Film 10x12 C.W.
Frontal Film 14x17 L.W.
Plane of Lateral Film
Lateral Cam
To target of Lateral Tube 43.2cm.
Axis of Lateral Film
45.3 cm.
Register Sockets for
Register Sockets for
Correction Factor for Frontal Film
cm. above plane of Frontal Film
Traveling Straight Edge
22.7 cm.
Plane of Frontal Film
Correction Factor for Lateral Film
28.2 cm.
cm. above plane of Lateral Film

Fig. 3. Top view of travelling straight-edge instrument for working up 90° triangulation films made by the jacket method. The working surface of the instrument is cork linoleum. The cams, film studs, register sockets, and scale are of brass; the travelling straight edge of aluminum. The correction factor is computed from Equation I (1). The distances between axes and planes of films and targets and planes of films are the same as those obtaining in our apparatus for the filming of pregnant women. Values can be varied to suit the needs of other workers.

devote himself entirely to the clinical aspect of the work, leaving to any reasonably intelligent stenographer or technician the routine working-up of films.

In the jacket method as employed by us at present, target-film distance (d) is 88.5 cm., the axis of the frontal film is displaced 28.2 cm. from the plane of the lateral film, and the axis of the lateral film 22.7 cm. from the plane of the frontal film. These values and certain others such as the distances between register points and optic axes can be changed to suit the needs of be the same as those obtaining at the time the films were made.

In the completed roentgenograms one punches register holes, identifies and marks the frontal film and the lateral film, locates by inspection the approximate centers of the shadows of the fetal skull, and marks these centers by pin pricks. For the living subject, films will usually be size 14 × 17 in., placed lengthwise, or for heavy women they may be placed crosswise. In experimental work, smaller films may be used with their axes in either direction. Figure

3 shows the instrument. Figure 4 is a composite drawing showing the lateral film in solid lines, the frontal film in partially dotted lines. It should be noted that actually the films are placed on the instrument one at a time, being shown together in this sketch merely to simplify explanation of technic.

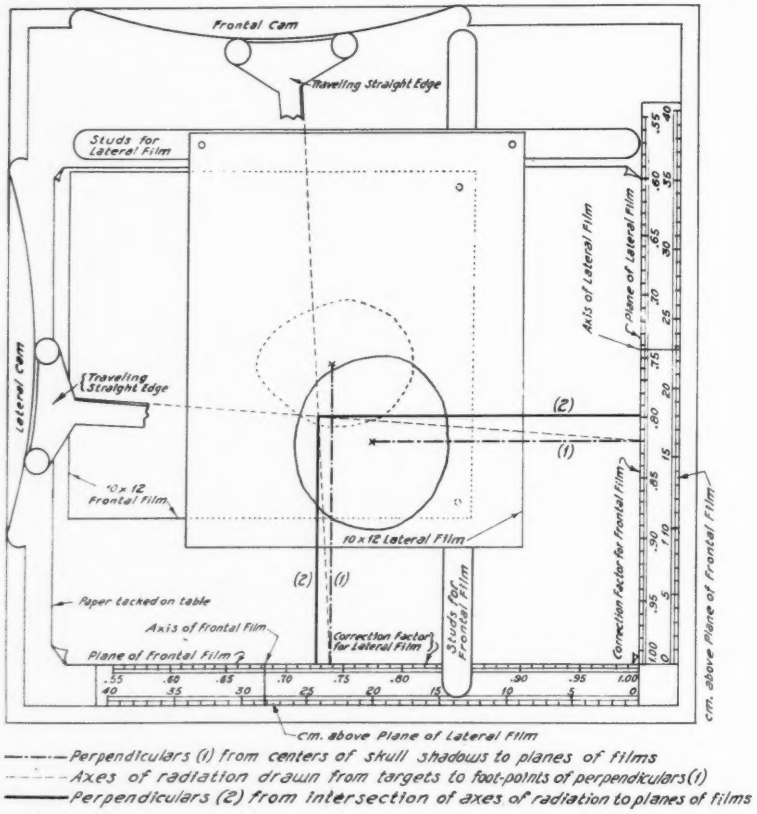
Frontal Cam
Travelling Straight Edge
Studs for Lateral Film
Axis of Lateral Film
Plane of Lateral Film
Lateral Cam
Traveling Straight Edge
(2)
(1)
10 x 12 Frontal Film
10 x 12 Lateral Film
Correction Factor for Frontal Film
cm. above Plane of Frontal Film
Paper tacked on table
Axis of Frontal Film
Plane of Frontal Film
Correction Factor for Lateral Film
Studs for Frontal Film
cm. above Plane of Lateral Film
—·—·— Perpendiculars (1) from centers of skull shadows to planes of films
- - - - - Axes of radiation drawn from targets to foot-points of perpendiculars (1)
——— Perpendiculars (2) from intersection of axes of radiation to planes of films

Fig. 4. Composite sketch illustrating the use of the travelling straight-edge instrument.

Drawing paper is pinned to the bed of the instrument. The lateral film is placed on the appropriate studs, a prick mark is made through the center of the skull shadow into the paper, following which the film is removed from the studs. Leaving the paper in place, the frontal film is placed on its studs and the process is repeated. We have now on the paper two pin pricks which are circled with lead pencil and identified as "the lateral center" and "the frontal center," respectively. With the aid of a triangle, perpendiculars are now dropped from the lateral center horizontally to the right to the plane of the lateral film and from the frontal center downward to the plane of the frontal film.

The foot-points of these two perpendiculars are known as lateral and frontal foot-points. The travelling straight edge having been placed against the frontal cam and rotated until it coincides with the frontal foot-point, a dotted line is drawn from this foot-point to the cam. Since this line indicates the path of the radiation at the time the frontal film was made, it follows that the center of the skull must have lain somewhere along it. The process is now repeated using the lateral cam and lateral foot-point, and by obvious rea-

soning it follows that the actual position of the center of the skull in space relative to the x-ray tube and films must be the crossing of these two dotted lines.[2]

From this point of crossing, new perpendiculars are dropped, one horizontally to the right to the plane of the lateral film, the other downward to the plane of the frontal film. This done, we may read at the foot-points of these secondary perpendiculars the height of the center of the skull above the plane of the frontal film (in case illustrated, 18 cm.) and above the plane of the lateral film (in case illustrated, 24.5 cm.). Knowing the value of these (d's) and knowing further that the D is fixed (88.5 cm.), we may, if we wish, turn to a graph of Equation I (1) and thus obtain the correction factors for both films. It is simpler, however, to have these factors engraved on the rule of the instrument so that instead of reading the height of the skull center above the films, one reads off the correction factors directly. Note that the factor for the frontal film is obtained from measurements in the plane of the lateral and the factor for the lateral film from measurements in the plane of the frontal.

As yet our principal use of the jacket method has been in experimental work with dead fetuses, but we have put it to some clinical use with fair success. The principal difficulty recognized at present is the fact that in the lateral view the fetus is sometimes excessively far from the film.

TEST OF VALIDITY OF MEAN CIRCUMFERENCE AS AN INDICATION OF FETAL AGE

Through the co-operation of Dr. Fred Adair and Dr. Edith L. Potter we have been able to examine a considerable number of the dead fetuses that are brought in from all over the city to be autopsied at the Chicago Lying-in Hospital. For this work we set up in a room adjacent to the autopsy room apparatus consisting of wooden supports for a lateral film and lateral tube, frontal film and frontal tube arranged with film axes, film planes and tube targets in the same relationship as in our travelling straight-edge instrument and in our clinical filming apparatus.

As a preliminary step, OFD was measured roentgenographically by a precise "position" technic which we shall not describe in detail at this time. Following this, the fetal cadaver was placed on a masonite supporting platform above the frontal film and in front of the lateral film. It was arranged that the distances from the skull center to the two films should be approximately the same as those obtaining in our raying of living objects, but we purposely avoided measuring these distances and did not arrange the skull for any particular angular relationship between the plane of its occipitofrontal axis and the plane of the film. Care was taken, however, to assure that the skull was not moved during the making of the two films. At the autopsy which followed, Dr. Potter cutting through the scalp at the frontal and occipital poles made direct caliper measurements of occipitofrontal diameter (OFD). In numerous cases the films obtained were not suitable for measurement because of skull defects or disease (all of the fetuses were stillborn) or because of technical difficulties occurring early in the experiment, but in 15 of the cases measurements could be made. These 15 cases were worked up on the travelling straight-edge instrument to obtain correction factors, and from the average corrected circumferences age was computed (1). Age was also computed from OFD (1). Under the conditions of this experiment our measurements of OFD may be accepted as extremely accurate, and so, except for the unavoidable factor of biological variation, the estimates of age based on the OFD are accurate. In Table I, column 6 shows the average corrected circumference of each skull; column 3 shows the probable age in weeks computed from the OFD, and column 4 the probable age computed from circumference. Column 5 shows the percentage of error in the estimate of age from circumference, assum-

[2] Actually these lines represent the edges of planes and the point of their crossing represents the end of the line, but for our purposes the third dimension may be ignored, with resulting simplification of explanation.

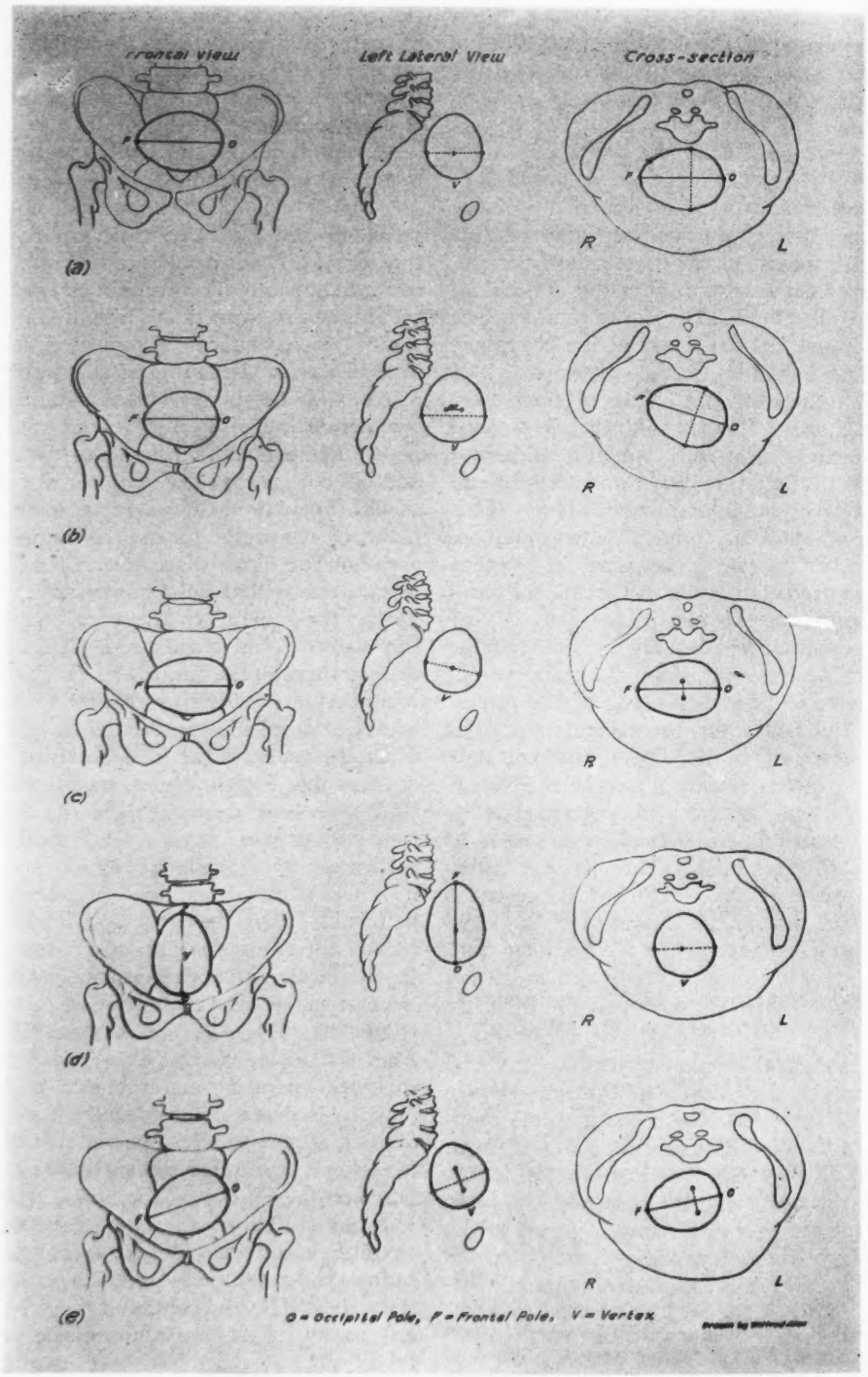

Fig. 5. (See facing page for explanation of plate.)

ing the values computed from OFD to be correct.

LIMITATIONS OF CIRCUMFERENCE AS A GUIDE TO SIZE OF SKULL AND AGE OF FETUS

In two-thirds of the 15 cases presented in Table I, the age predicted by circumference was correct or too great. In one-third of the cases it was too small. Numerous technical factors presumably combined to cause the smaller + and − errors but almost certainly the largest + error (11 per cent) was produced by lack of parallelism between the plane of the occipitofrontal axis of the skull and the plane of radiation common to the two x-ray tubes.[3]

The scope and limitations of roentgenographic measurements of occipitofrontal diameter, biparietal diameter and circumference as indicators of skull size are illustrated in Figure 5. In 5-*a* and 5-*c* all three measurements are valid. In Figure 5-*b* conditions are satisfactory for measurements of circumference but not for occipitofrontal diameter or biparietal diameter. In Figure 5-*d* measurements of occipitofrontal diameter and biparietal diameter are dependable but circumference is not. In Figure 5-*e* all three measurements fail.

To recapitulate:

(1) Occipitofrontal diameter can be measured only when the occipitofrontal axis of the fetal skull lies in a plane approximately parallel with the plane of the film. Obliquity of the axis relative to the film foreshortens the measurement and thus predicts too small an age.

(2) Biparietal diameter can be measured only when the biparietal axis lies in a plane approximately parallel with the plane of the film. As in the case of the occipitofrontal diameter, obliquity of the biparietal axis relative to the plane of the film foreshortens the measurement and thus predicts too small an age.

(3) The circumference of the skull of a fetus *in utero* (that is, the average net circumference taken from two films made at right-angles to one another) may be used in connection with graph No. 21 (1) of Equation 17A (1) for estimation of fetal age only when the occipitofrontal axis lies in a plane approximately parallel with the transverse plane of the body of the mother. Obliquity of the occipitofrontal axis rela-

[3] In our clinical apparatus only one tube is used, tube and film are fixed for the two exposures, but the patient turns between them. Under such conditions the surface of reference is a plane perpendicular to the plane of the long axis of the patient's body, referred to for convenience as the "transverse plane of the body."

Fig. 5. Effect of obliquity of skull upon roentgenographic measurements of circumference, occipitofrontal diameter, and biparietal diameter.

a. Vertex down, right parietal region looking forward in the frontal view. The occipitofrontal axis (shown as a solid line) lies in a plane parallel with the transverse plane of the body and parallel with the frontal film. The biparietal axis (shown as a dotted line) lies in a plane parallel with the plane of the lateral film. Under these circumstances all three measurements can be made: occipitofrontal diameter in the frontal film, biparietal diameter in the lateral film, and circumference from the combination of the two.

b. Vertex down, right parietal region looking obliquely forward and to the right in the frontal view. This causes both axes to be oblique to the film in both frontal and lateral views and accordingly makes them unsatisfactory for measurement. The occipitofrontal axis remains parallel with the transverse plane of the body, however, and so the mean of the circumferences as measured in frontal and lateral films can be used for estimating the age of the fetus.

c. Vertex down, left parietal region looking forward and downward in the frontal view; occipitofrontal axis parallel with the transverse plane of the body; skull rotated slightly about the occipitofrontal axis so that the vertex looks slightly backward. In the frontal view occipitofrontal diameter can be measured; in the lateral view, biparietal diameter; from the combination of the two, circumference.

d. Fetal head flexed sharply on neck so that vertex looks directly forward in the frontal view. In both frontal and lateral views occipitofrontal axis is parallel with the plane of the film, and in the frontal view the biparietal axis is parallel. This means that biparietal diameter can be measured in the frontal film and occipitofrontal diameter in either of them. The occipitofrontal axis is not parallel with the transverse plane of the body; instead, it is rotated as far as possible out of this parallel relationship or, in other words, stands at 90° to the transverse plane. As a result of this, circumference cannot be used as a guide to fetal age.

e. In the frontal view vertex directed downward, forward, and to the left; left parietal region directed forward, upward, and to the left. In skew positions of this sort where the occipitofrontal and biparietal axes are not parallel with the film in either view and where the occipitofrontal axis is not parallel with the transverse plane of the body, no one of these three criteria of fetal age can be employed with accuracy. In the case of circumference the difficulty is fundamental in the theory involved while in the case of the two axes it depends upon the fact that such positions fail to throw the end-points of the axes into silhouette, a condition essential to their accurate identification.

TABLE I.—TEST OF VALIDITY OF MEAN CIRCUMFERENCE AS AN INDICATION OF AGE

Material	Occipitofrontal Diameter		Age		Percentage Error of Estimate from Circumference	Circumference
	Caliper	X-ray	From OFD	From Circum.		
A-1	6.4	6.4	21 3/4	22	+ 1.15	17.6
A-2	11.5	11.5	37	36 1/4	− 2.00	30.25
A-3	10.9	10.85	35 1/4	36	+ 2.13	30.24
B-1 } Twins	6.5	6.8	22 3/4	23 1/2	+ 3.30	19.23
B-2 } Twins	7.1	7.3	24	25	+ 4.20	20.46
B-3	10.3	10.46	33 3/4	33 1/2	− 0.70	28.1
B-4	11.0	11.2	35 3/4	39	+11.00	32.24
B-5	9.7	9.6	31 1/4	32 1/4	+ 3.15	27.16
C-1 } Twins	6.4	6.3	21 1/2	21 3/4	+ 2.32	17.24
C-2 } Twins	6.6	6.6	22 1/4	22 1/2	+ 1.12	18.0
C-3	6.0	6.1	21	20	− 4.76	15.28
C-4	9.3	9.3	30	28 1/2	− 5.00	23.9
C-5 } Twins	7.5	7.1	23 1/2	23 1/2	0	19.25
C-6 } Twins	7.1	7.0	23 1/4	24	+ 3.22	19.54
C-7	9.8	9.6	31	29 3/4	− 4.00	24.8
Column Number	1	2	3	4	5	6

tive to the transverse plane of the body increases the value of the average circumference and thus predicts too great an age. In the extreme case where the axis lies 90° to the tranverse plane, frontal circumference and lateral circumference are equal and the predicted age is much too great.

One who attempts to determine the age of a fetus *in utero* from measurements of the roentgenograms must exercise judgment. In those cases in which conditions for measurement are good, age estimates should be given out with confidence and looked upon as accurate within the limitation of biological variation (in the majority of cases, + or − two weeks). When a preliminary study of roentgenograms shows an occipitofrontal axis slightly oblique to the plane of the film and to the transverse plane of the body, errors in prediction are inevitable. If circumstances make it necessary that a prediction be attempted, the difficulties of measurement should be described in the report and it should be recognized that if age is being predicted from occipitofrontal diameter the prediction is probably too small; if from circumference, probably too large. In certain skew positions of the skull one must recognize that he cannot employ circumference as a guide to age.

Skewness of any type or degree might be present without interfering with measurement of occipitofrontal diameter or biparietal diameter by means of the measuring stereoscope or the stereoroentgenometer if the end-points of the axis could be located accurately. In most cases, however, the end-points cannot be identified with accuracy unless the plane of the axis is approximately parallel with the plane of the film.

SUMMARY

(1) An improved jacket for the making of 90° triangulation films and an instrument for working up such films are described.

(2) The usefulness of skull circumference as a guide to fetal age is demonstrated by experiments on 15 fetal cadavers.

(3) The limitations of occipitofrontal diameter and biparietal diameter as indicators of fetal age are discussed.

(4) It is pointed out that like these other two measurements skill circumference has its limitations as a guide to fetal age.

REFERENCE

(1) HODGES, PAUL C.: Roentgen Pelvimetry and Fetometry. Am. Jour. Roentgenol. and Rad. Ther., May, 1937, **37**, 5.

THE USE OF INTERSTITIAL RADIATION IN THE TREATMENT OF PRIMARY AND RECURRENT CARCINOMA OF THE UTERINE CERVIX[1]

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IN many clinics there is a tendency to standardize the treatment of cervical cancer so that a routine method of radiation is used for all patients. No single method is suitable for all individuals, but in most instances there are certain advantages to be gained if treatment is begun with external radiation (8). By that means the amount of infection in the lesion can be reduced, which, in turn, will lessen the local reaction from radium applied at a later date. A preliminary course of x-rays also facilitates radium treatment by producing some regression in the size of the primary lesion. However, if the percentage of cures is to be increased materially, it is essential to individualize both the roentgen and radium treatment of each patient to meet the requirements of the lesion in question, rather than to apply a single method to all patients with cervical cancer.

In a previous publication (2) diagrams illustrating the distribution of roentgen radiation within the average female pelvis were given for different physical factors of radiation. In the treatment of carcinoma of the cervix it is essential that a large dose be given to the parametrium without over-radiating normal structures in other regions. A six-field technic (two on the anterior surface, two on the posterior, and one on each lateral aspect of the pelvis) was found to deliver the greatest amount of radiation to the parametrium without too great a percentage of the total dose falling upon the bladder and rectum. That arrangement of skin portals is suited to most patients with cervical cancer, but in every instance the attempt should be made to individualize the treatment. A different technic might be more practical for patients presenting a marked degree of involvement anterior or posterior to the cervix.

There is general agreement that an intra-uterine tandem containing radium will not control disease located at distances greater than 3 or 4 cm. from the cervical canal. In the attempt to increase the radius of effect from radium applied to the primary lesion, Healy (6) and others have devised various intra-vaginal applicators for use in conjunction with an intra-uterine tandem. In most patients, however, radium alone is inadequate for delivering a lethal dose to the entire tumor-bearing region. External radiation is essential in the attempt to treat adequately the disease located in outlying tumor-bearing areas, and in the deep lymphatics.

The distribution of radiation for different methods of applying radium to the cervix has been shown diagrammatically by Lucas (10) and the author (1). While these diagrams show that radium alone is inadequate for most patients, they also illustrate the fact that a greater number of sources of radium distributed more widely throughout the uterus and vagina will, for specified doses, increase the *minimum* amount of radiation reaching the tumor, and decrease the risk of over-radiating some regions. It is obvious that normal structures must be protected from doses that will result in permanent damage, but it should be noted also that the *minimum dose* is even more important than the *maximum amount* of radiation delivered to a given volume of tissue. If the dose reaching some parts of the tumor is less than the amount required for producing a lethal effect upon the disease, that portion of the tumor will recover from the tempo-

[1] Presented before the Fifth International Congress of Radiology, at Chicago, Sept. 13–17, 1937.

rary effect of the treatment and then continue to grow. A greater percentage of the volume of tissue in question will receive an adequate amount if the minimum dose delivered throughout that volume is increased.

The most logical means of distributing a greater number of sources of radium more widely throughout the tumor-bearing area is by means of interstitial radiation, such as needles, seeds, etc. For a number of years Ward (14) has combined needles with an intra-uterine tandem in the primary treatment of cervix cancer. The needles were usually inserted into the cervix in a radial fashion around the tandem. Healy (7) has implanted gold radon seeds into some patients with recurrent or persistent disease in the cervix and adjacent areas. Gellhorn (5) has reported the use of gold seeds in the parametrial regions. Taussig (13) performs lymphadenectomy after radiation, or implants seeds into the nodes or into regions occupied by the various lymph glands.

Other authors both here and abroad have reported the use of interstitial radiation, but for the most part gynecologists in this country have been reluctant to employ such methods. This has been at least partially due to the fear of introducing infection into the tumor by the insertion of needles and seeds, and to the fear of excessive reactions following such treatment. However, those complications were not found to be frequent sequelæ in the large series of patients with cervical cancer reported recently by Pitts and Waterman (11). Their statistics covered two periods of five years each. During the first period treatment was given at relatively high intensities by means of radium placed in the uterus and in the vagina (in many patients relatively strong steel needles were also used interstitially in the cervix). Total doses ranged from 3,000 to 4,000 mg.-hr. These were administered in two or three applications made from two to three weeks apart. In 1926, which marked the beginning of the second five-year period of their published statistics, treatment was given at lower intensities over longer periods of time (for a single application) by means of weak interstitial sources in both the cervix and parametrial regions. They used platinum needles containing relatively small amounts of radium (2.0 to 4.0 mg.), with active lengths ranging from 30 to 45 mm.

When they first began to use interstitial sources routinely, the needles were inserted into the cervix, paracervical tissues, and parametrium, by introducing them through the vagina, and intraperitoneally through an abdominal incision. They later abandoned the intra-abdominal route. The general plan of their treatment was to place two needles (each containing 3.0 mg. radium) into the parametrium along the right side of the uterus, and two similar needles into the left side. A total of from 12 to 16 needles (2.0 mg. each) were inserted into the anterior and posterior lips of the cervix and para-cervical tissues. A tandem, usually containing 20 mg., was placed in the uterus. The radium was left in place for periods ranging from 72 to 96 hours, but during the last two years of their published statistics the time of radiation was from 144 to 168 hours. This indicates that some patients received approximately 10,000 mg.-hr. of irradiation over a period of seven days.

For the second five-year period (during which needles were employed), the authors report an absolute five-year survival of 31.7 per cent, as compared with 20 per cent for their older method. Furthermore, analysis of their statistics showed an absolute five-year survival of 36.3 per cent for the longer time of irradiation (144 to 168 hours), as compared with 21.8 per cent for the shorter time (72 to 96 hours). The uncorrected mortality following the use of needles was 2.9 per cent, and the incidence of fistulæ was 6.3 per cent.

Their uncorrected mortality rate, which may be higher than that experienced in most clinics, seems justified in view of the fact that their statistics show so much improvement over those usually reported. The authors experienced little difficulty

from infection resulting from the introduction of needles, and evidently local reactions were not beyond the limits of repair.

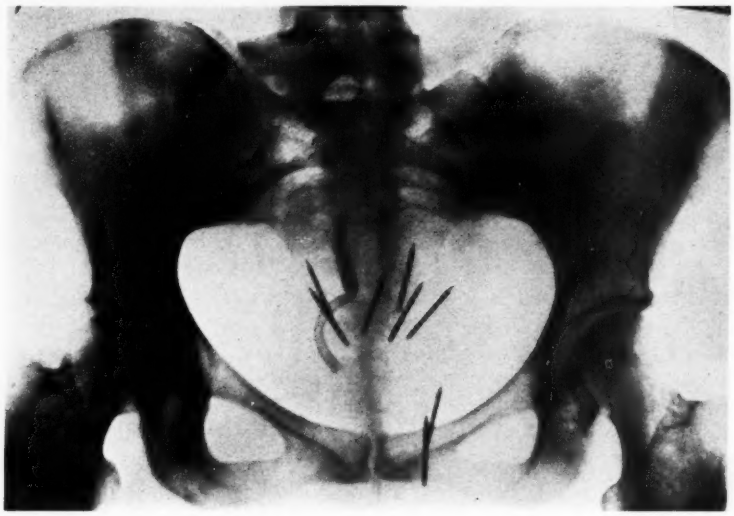

Fig. 1. Location of an intra-uterine tandem composed of three capsules containing 25 mg. radium each with a filter equivalent to 0.5 mm. Au, and steel needles of 12.5 mg. strength used in the palliative treatment of a patient with a recurrent lesion involving the cervix and vaginal vault, and an isolated metastatic nodule in the left wall of the vagina. The curved and lighter shadow is formed by rubber tubing around the intra-uterine sources.

Their excellent statistics show clearly that interstitial radiation is of value in the treatment of cervical cancer. They concluded that the method was particularly valuable in the treatment of Stage III (Schmitz) cases, which, of course, represent patients with disease located at distances beyond the radius of effect of radium inserted into the cervical canal and uterine cavity.

During 1936 we began to use interstitial radiation in some patients with cervical cancer. For the earliest treatments we selected those with recurrent lesions. They were chosen for two reasons: in the first place, the method was, in our hands, an experimental procedure, and it was believed essential to proceed by a process of trial and error on patients with a poor prognosis in the attempt to determine the amounts of radiation the regions involved would tolerate. In the second place recurrent lesions were for various reasons suited to treatment with interstitial radiation. Control of the disease usually requires relatively large amounts of radiation, because the character and radiosensitivity of the tumor have been altered materially by the earlier treatment. At the same time care must be exercised in administering additional amounts of radiation, because of the risk of causing the previously radiated tissues to break down with necrosis and slough. The dose delivered to the diseased area by means of external radiation is usually inadequate for producing any permanent change in the tumor, and in many instances that method may not be practical due to the condition of the skin in the fields used previously. Radium applied to the uterus, or in the vagina, if used in amounts considered adequate for controlling the disease within a radius of 3.0 or 4.0 cm., is apt to over-radiate the tissues nearest to the application and produce a persistent ulcer. Interstitial radiation presents a means of at least partially overcoming some of the above-mentioned difficulties. The more uniform distribu-

tion of radiation from multiple buried sources lessens the discrepancy between the minimum and maximum dose arriving throughout the diseased area. By that means it is possible to deliver a reasonable dose at points located a few centimeters deep without enormously greater amounts arriving at the surface of the cervix and vaginal vault, or in the uterine canal.

Fig. 2. Location of radium used in the primary treatment of a patient with a very advanced and cratered lesion. Three capsules containing 25 mg. each were arranged in a triangular fashion and packed into the shallow uterine cavity. Eight steel needles of 12.5 mg. strength were inserted in a radial fashion within the inner half of the radius of the crater.

At first the treatment was applied to those with disease reappearing only in the cervix itself, because a recurrence of that type indicates inadequate primary radiation and, therefore, there should be a minimum of risk in administering additional amounts. The method was later extended to include patients with more extensive recurrences, and recently it has been employed in the primary treatment of some individuals. Sufficient time has not elapsed to permit a statistical report upon the results obtained. However, a description of the method is justified in view of the excellent response of many lesions.

Before any patient has been treated with interstitial sources a suitable tissue dose has first been determined. A plan has then been worked out for inserting the needles in a manner to deliver the most suitable distribution of the predetermined dose. Data for the arrangement of interstitial sources, and the number of milligram-hours of radium required for treatment have been taken from publications by Quimby (12) which give the amount of radiation required for delivering various threshold doses to specified volumes. It should be noted that some recurrent cases were deliberately undertreated, due to the fact that the additional radiation was given for palliative purposes only. In many instances it was deemed advisable to attempt no more than to relieve pain or promote the healing of an ulcerated area.

In Figure 1 is shown a radiograph illustrating the location of needles used in the treatment of a patient with a recurrent

lesion. Due to metastases present in the lungs and supraclavicular nodes that had not responded satisfactorily to external radiation, the additional radium was given only as a palliative measure in the attempt to control bleeding from ulcerations on the cervix, vaginal vault, and on the left lateral wall of the vagina. For that purpose a minimum of four or five threshold doses was considered adequate. Treatment was administered by means of six steel needles (12.5 mg. radium each) inserted into the cervix and left vaginal fornix around an intra-uterine tandem composed of three capsules containing 25 mg. each. As can be seen in the radiograph, the sources were relatively far apart. Two additional needles of the same strength were inserted into the separate vaginal nodules. For the specified arrangement of radium in the cervical region, and the volume of tissue to be treated, approximately 2,000 mg.-hr. were required for delivering the predetermined minimum of four or five threshold doses. There was only a mild reaction, and the treatment was adequate for promoting healing of the ulcerated areas, which controlled the bleeding until the patient's death a few months later resulting from the distant metastasis present before radium was applied.

In spite of the inadequate filter and relatively large radium content of the needles described above, they have been used for greater doses in some instances. For example, in Figure 2 is shown a radiograph illustrating their use in the primary treatment of a patient presenting a particular problem. The disease was very extensive, and a huge, badly infected and ulcerated crater replaced completely the cervix, vaginal vault, and the lower portion of the uterus. It was possible to see directly the entire uterine cavity, which was only 3.0 cm. deep. There was also a vesico-uterine fistula. After a preliminary course of external irradiation[2] it was decided that radium should be given in two applications so that the dose from any needle at any given time would not exceed 150 mg.-hr. At each application approximately 2,000 mg.-hr. were administered by means of three 25 mg. capsules arranged in a triangle and packed into the shallow uterine cavity, and eight 12.5 mg. needles inserted in a radial fashion within the inner half of the radius of the crater. The treatments were given two weeks apart.

From both x-rays and radium the central pelvis received a minimum of from six to eight threshold doses. The outlying tumor-bearing regions received a minimum of about three or four threshold doses. The latter amount will rarely produce a lethal effect upon cervical cancer, but a fairly large volume of the more centrally located disease was radiated adequately, as evidenced by regression in that region. It is doubtful if radium placed only in the uterine cavity and vagina could have been used safely for delivering an equal minimum dose to the same volume of tissue. However, the patient presented a hopeless prognosis. She died some time later with uremia due to obstruction of both ureters.

Sheath needles for removable platinum cells containing different amounts of radium have been found to be more satisfactory than the above-mentioned sources. This is not only the result of the heavier filter and the lower intensity of radiation, but also due to the variety of changes that can be made in the length and strength of sources. In Fig. 3 is shown a radiograph illustrating their use in a patient with a hard nodular recurrence in the left parametrium which had extended along the anterior vaginal wall and infiltrated the base of the bladder. Treatment was administered in the attempt to relieve the bladder distress, but it was feared that the dense avascular tissue might break down. For that reason a method of treatment was planned that would deliver a minimum of three threshold doses, without amounts greatly in excess of that arriving at points more than 0.5 cm. from any particular implant. The predetermined dose was ad-

[2] A short course of roentgen treatment was employed instead of a prolonged series of divided doses. Due to the risk of pelvic peritonitis and other complications, we have abandoned the longer method in patients with very extensive and badly infected lesions.

ministered by inserting four needles of 6.6 mg. strength with an active length of 2.0 cm. into the cervix and left parametrium, and seven needles of 1.0 mg. strength with right parametrium extending into the region of the right ureter. Additional treatment was administered, but sufficient time has not elapsed to determine the degree of

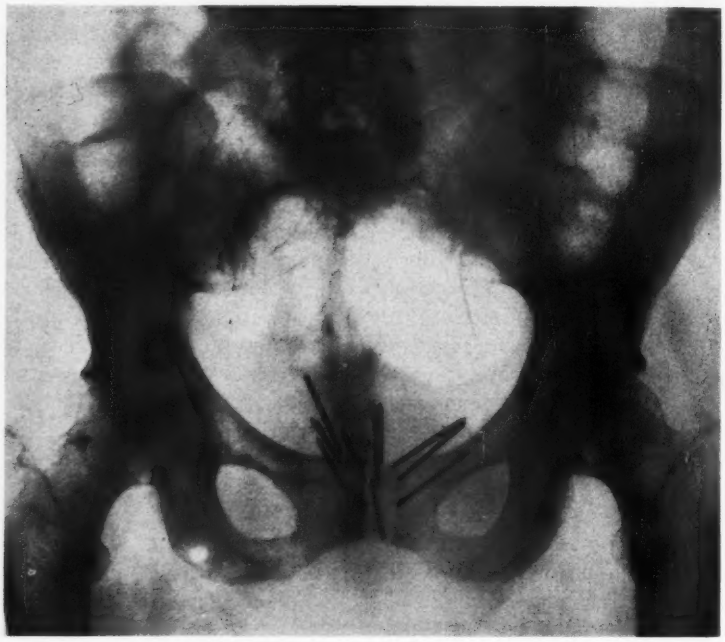

Fig. 3. Arrangement of sheath needles holding platinum cells (total filter equivalent to 0.5 mm. Au) employed in the treatment of a patient with a hard, nodular recurrence involving the left parametrium and extending along the anterior vaginal wall into the base of the bladder. The longer needles have an active length of approximately 2.0 cm. and contain 6.6 mg. radium each. The shorter needles are 1.0 mg. strength with an active length of approximately 1.0 cm.

an active length of 1.0 cm. into the anterior vaginal wall. The stronger needles were removed after 48 hours, but the weaker sources were used for five days (120 hours). The total dose was approximately 2,100 mg.-hr. There was very little evidence of reaction following the treatment, and consequently there was only slight evidence of regression. However, the degree of palliation was satisfactory, and the bladder symptoms were relieved. Seven months after treatment the patient complained of pain in the back and in the left pelvis. This was attributed to obstruction and dilatation of the left ureter, noted cystoscopically and radiographically. There was also beginning involvement of the palliation that will be obtained. The function of the right kidney has remained adequate, and the patient has been comfortable.

Due to their lower intensity of radiation, relatively weak sheath needles may be used to deliver doses considerably greater than those obtained from the stronger and more lightly filtered steel needles. Weak sources several centimeters in length implanted into the parametrial region can be used for doses far greater than the amounts reaching those regions from radium placed in the uterus and the vagina. However, the needles must be implanted with care and in a manner that will irradiate the entire region. In Figure 4 is shown a radiograph illustrating a rather

careless and irregular arrangement of interstitial sources used in the treatment of a patient with a large mass in the right parametrium.

Fig. 4. An irregular arrangement of interstitial sources used in the primary treatment of a patient with a large mass in the right parametrium. The shorter needles, 2.0 mg. radium each, have an active length of approximately 2.0 cm. The two longer needles are approximately 6.0 cm. in length and contain 5.5 mc. radon. The intra-uterine tandem is composed of three capsules containing 25 mg. radium each. All sources have a filter equivalent to 0.5 mm. Au.

This patient had a small, non-ulcerated primary lesion which had not caused any enlargement of the cervix. There was no clinical evidence of involvement in the left parametrium, but there was a large, irregular mass at least 5.0 cm. in diameter on the right side that bulged into the vaginal fornix and held the uterus in a fixed position. There was little evidence of regression following the administration of from two to three threshold doses throughout the pelvis by means of external irradiation. Radium was applied two weeks after the completion of x-rays, and it was deemed necessary to deliver an amount that would bring the minimum tissue dose to at least six to eight threshold doses. Since there was no clinical evidence of involvement in the left parametrium, it was believed that an intra-uterine tandem and x-rays should be adequate for controlling the disease in that region. However, a method other than the placing of radium in the uterus or vagina was necessary for delivering the predetermined minimum dose to the right side. Treatment was administered by means of 10 needles of 2.0 mg. strength with an active length of 2.0 cm. and two needles 6.0 cm. long containing 5.5 mc. radon each. The interstitial sources were used for a period of five days and delivered equivalent of 3,300 mg.-hr. An intra-uterine tandem was used for 3,000 mg.-hr. The total radium dose was, therefore, 6,300 mg.-hr. For the arrangement of sources and the volume of tissue treated, that amount of radiation combined with x-rays represented a minimum of from six to eight threshold doses. The mass on the right side regressed completely with the exception of a small region near its upper border. The persistent disease was prob-

ably located medial to the long radon needles, and above the points of the shorter radium needles. The patient has been observed for one year, and the residual mass has not increased in size. There was no reaction following treatment except rather severe cystitis, which was controlled by frequent bladder irrigations and medications.

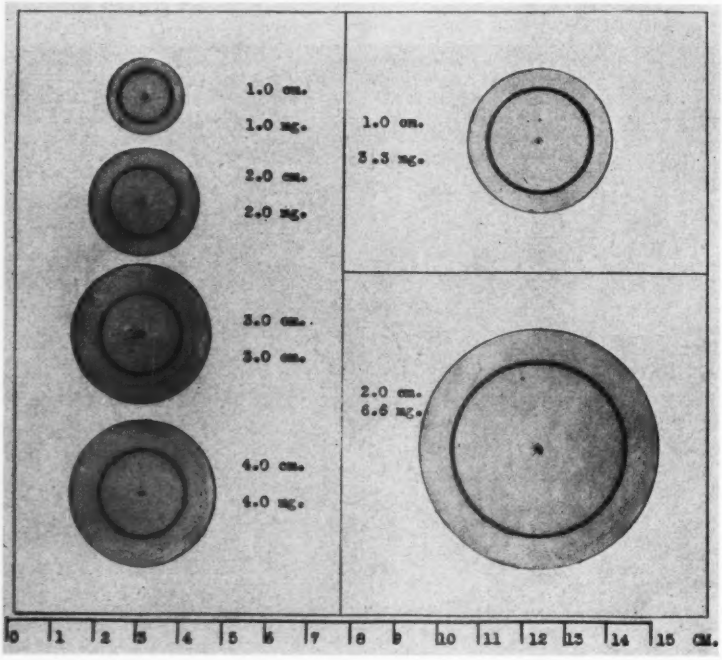

Fig. 5. Isodose charts prepared from radiographic film for needles with 0.5 mm. Au filter of specified lengths and strengths. The curves illustrate the distribution of different threshold doses along a line perpendicular to the middle of each source for 133 hours' radiation (1.0 mc.-destroyed per milligram strength). The distribution of one threshold dose is indicated by the periphery of each disk. The curve for two threshold doses has been scratched upon the film by means of dividers and the groove colored with ink.

The film of this patient is shown primarily to illustrate the importance of a predetermined tissue dose and method of treatment. The lack of a definite plan for inserting the needles can be seen readily in the radiograph. While the end-result was better than had been expected, a portion of the disease was irradiated inadequately because of the careless distribution of the sources. It is, of course, impossible to implant needles with exact precision, but in every instance it is essential to employ a method that will deliver the most suitable distribution of radiation for the lesion under treatment. In general, the therapy failures have been more instructive than the successes, and the patients discussed here have been selected to illustrate the value of interstitial radiation in cases of primary and recurrent carcinoma of the cervix presenting particular problems in treatment. If in every instance the treatment is carefully planned and individualized for the patient in question, it can be administered without risk of severe injury or other complications.

The planning of treatment for a given individual can be divided into three important steps. One must first decide upon a minimum tissue dose considered adequate for the lesion in question. It is

then essential to devise a method of treatment which will deliver a distribution of radiation suited best to the volume of tissue to be irradiated. Finally, one must know how much radiation is necessary to deliver the predetermined tumor dose.

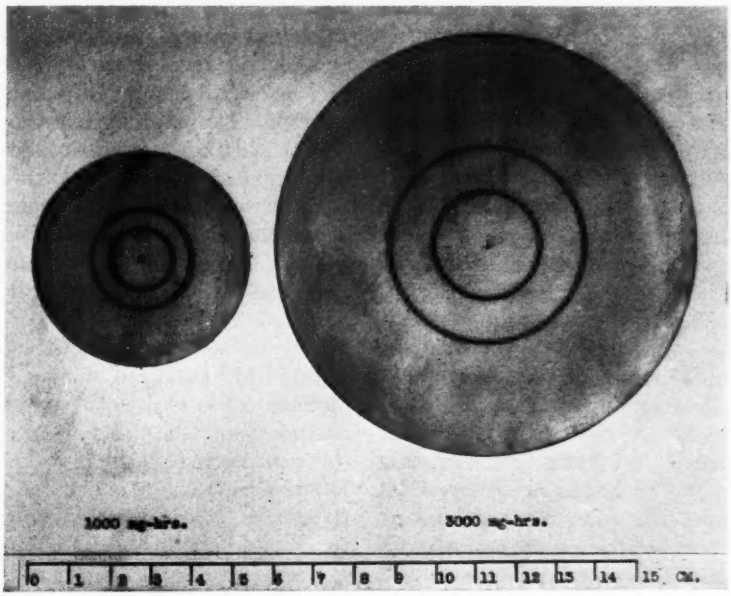

Fig. 6. Isodose disks showing the distribution of one, four, and seven threshold doses from an average intra-uterine tandem with 0.5 mm. Au filter for 1,000 and 3,000, mg.-hr. radiation.

In general, greater tissue doses will be employed in the primary irradiation of a patient than in the treatment of a recurrent case, or one with very advanced disease in whom nothing more than palliation can be expected. There is evidence that, for specified methods of treatment, control of the disease in carcinoma of the cervix requires a *minimum* of from six to eight threshold doses (3, 9). The relation of five-year survivals to calculated tumor doses has been shown recently by Frazell (4). Relatively few patients were cured when some portions of the tumor received less than three threshold doses. The percentage of survivals was found to increase among patients who had received greater amounts of radiation. The author concluded that a method delivering a minimum of less than three threshold doses was relatively ineffective, and suggested that interstitial radiation, whenever practical, should present a method for increasing the quantity of radiation reaching the parametrial regions.

In the attempt to deliver a distribution of radiation suited best to the volume of tissue in question, it is essential that a number of different methods for applying radium be considered in planning the treatment of every patient. The addition of interstitial radiation to other procedures which may be employed increases the number of methods from which one may choose. In many patients, buried sources may present the most practical means of individualizing the treatment. Statistics presented by others illustrate the clinical value of interstitial radiation in the treatment of cervical cancer. The physical value of the method is evident from the fact that a number of weak sources are distributed throughout the tumor-bearing region. By that means it is possible to increase the *mini-*

mum dose delivered to the diseased area without administering excessive amounts from any particular source.

For determining the amount of radiation necessary to deliver a predetermined dose for a given arrangement of radium, it is necessary first to estimate the volume of the region in question, and then consult tables published by Quimby (12) showing the amount of radiation required for delivering various threshold doses to specified volumes. Such procedures are sometimes complex, and for cervical cancer the degree of accuracy is not great, because of the large volume of the tumor-bearing region, the difficulty of determining its dimensions, and the differences in strength of source which must be used (*i.e.*, tandem, needle, etc.). In many patients it is necessary to plan the treatment upon the physical principles of interstitial radiation and consider the effect of length, strength, filter, distance, etc., upon the dose arriving at various points from each source. In such instances the approximate size and location of the region in question is indicated upon a diagram, and the distribution of radiation calculated for different arrangements of needles, tandems, special applicators, etc., in the attempt to determine the method best suited to the treatment of that individual.

Those procedures are both tedious and complex. As an aid in calculating tissue doses, isodose charts were prepared for interstitial sources which can be used for radium in the same manner as depth dose charts prepared by others have been used for x-rays. However, instead of showing percentage depth doses the curves for radium were drawn to indicate the distribution of various threshold doses along a line perpendicular to the middle of the source. In view of the fact that the isodose curves were drawn for threshold doses instead of relative amounts arriving at various depths, it was necessary that each chart be prepared for a specified number of milligram-hours' radiation. In order that the curves for different sources might be compared, the dose was standardized by employing a definite period of time: for that was chosen 133 hours. Therefore, each set of curves represents the distribution of threshold doses for 1 mc.-destroyed per milligram strength of the source in question.

Isodose charts were first prepared for a number of needles with different active lengths and containing different amounts of radium. The sources selected for charts were chosen from various sheath needles holding platinum cells that might be used in the treatment of gynecologic carcinoma. Data were taken from publications by Quimby (12) for calculating the depths that various threshold doses are delivered by specified sources for 1 mc.-destroyed per milligram strength. Since the distribution of radiation is shown along a line perpendicular to the middle of each implant the curves about that point form a circle, and the isodose charts appear as circular disks. For practical use it is convenient to make them from discarded radiographic film as shown in Figure 5.

Due to the rapid falling off of intensity within a few millimeters of each source, it is impractical to indicate on the disks more than one or two isodose curves. The outer edge of each disk has been used to indicate the distribution of one threshold dose, and by means of dividers an inner circle has been scratched on the film to show the distribution of two threshold doses. The distances to which the different doses are

TABLE I.—NEEDLES

Active Length (cm.)	Strength mg. Radium	Total mc.-destroyed	Distance Threshold Doses Delivered (cm.)	
			1 T.D.	2 T.D.
1.0	1.0	1.0	0.9	0.6
	3.3	3.3	1.7	1.2
2.0	2.0	2.0	1.3	0.8
	6.6	6.6	2.8	2.0
3.0	3.0	3.0	1.6	0.9
4.0	4.0	4.0	1.7	1.0

Distances that one and two threshold doses are delivered along a line perpendicular to the middle of different needles with 0.5 mm. Au filter. The active length and radium content of each source is specified. Calculations are made upon the basis of 1 mc.-destroyed per milligram strength.

delivered by the various needles for specified amounts of radiation are given in Table I.

Similar isodose charts were also prepared for intra-uterine tandems. Due to the fact that radium applied within the uterus is usually employed for a relatively large amount of radiation it is practical to indicate upon each chart the distribution of one, four, and seven threshold doses. However, tandems frequently contain more radium than would justify their use for 133 hours. It was believed impractical to apply the same standardization of dose employed for needles. Instead of drawing isodose curves for 1 mc.-destroyed per milligram strength, the charts were prepared for a specified number of milligram-hours' radiation. In order to provide some variation in dose, isodose disks were made for average intra-uterine tandems delivering 1,000 mg.-hr., and 3,000 mg.-hr. as shown in Figure 6. The distances to which different threshold doses are delivered along a line perpendicular to the middle of the tandem for the specified amounts of radiation are shown in Table II. For pre-

TABLE II.—TANDEMS

Dose in mg.-hr.	Total mc.-destroyed	Distance Threshold Doses Delivered (cm.)		
		1 T.D.	4 T.D.	7 T.D.
1,000	7.5	2.6	1.2	0.8
3,000	22.5	5.2	2.4	1.8

Distances that one, four, and seven threshold doses are delivered along a line perpendicular to the middle of an average intra-uterine tandem with 0.5 mm. Au filter for 1,000 and 3,000 mg.-hr. radiation.

paring the disks data were taken from an earlier publication upon the distribution of radiation for different methods of applying radium to the cervix (1). Diagrams presented in the article referred to can be used, if drawn to actual size, in conjunction with the isodose disks here shown for determining tissue doses from various combinations of needles, intra-uterine tandems, and intra-vaginal applications of radium for specified amounts of radiation. The disks can be superimposed over a diagram illustrating a lesion to be treated, and the approximate tissue dose determined for any given arrangement of radium. If a source is used for double the dose, then two threshold doses will arrive at the circle indicating one, but for the greater number of milligram-hours one threshold dose will not arrive at twice the distance, but at a point which received 0.5 threshold dose.

Despite the fact that the curves were prepared from data published by Quimby, the standard dosage tables she has given cannot be dispensed with unless disks are prepared for each dose for which a given source may be used. A reasonable knowledge of the standard data is essential, but with a little practice it is possible to arrive at tissue doses from the disks that are in good agreement with those calculated from the tables.

The isodose curves have proven to be useful aids in teaching the principles of interstitial radiation. They present a fairly rapid method for determining the amounts of radiation required for delivering a predetermined tissue dose considered adequate for a given lesion. Furthermore, use of the disks necessitates a careful planning of radiation that insures individualization of treatment.

Interstitial radiation has been demonstrated to be of value in the treatment of both primary and recurrent carcinoma of the cervix. As stated before, objections to the use of buried sources have been based chiefly upon the fear of introducing infection, and of producing severe reactions. The use of preliminary external radiation is undoubtedly an important factor in diminishing the risk of infection (8). It seems likely that some of the severe reactions noted earlier by other gynecologists may have been due to the use of relatively strong and inadequately filtered needles (*i.e.*, short steel or monel metal needles with an active length of 3.0 cm. or less, and containing 10.0 or more milligrams radium). The lower intensity from adequately filtered sources containing relatively small amounts of radium (for ex-

ample, gold or platinum sheath needles holding one or more cells containing 1.0 or 3.3 milligrams radium each) is probably of importance in reducing the risk of severe tissue reactions. However, the most important factor in the prevention of untoward sequelæ following the use of interstitial radiation, or any other method of applying radium is the careful planning of the treatment for each patient.

To avoid accidents and reduce the number of failures of treatment it should be emphasized that it is essential to decide first upon a predetermined dose considered adequate for the lesion in question, and then to apply that amount by a method which will deliver a distribution of radiation suited best to the volume to be radiated. It should be noted here that estimations of tissue dose can be only approximate, and by no means can radium be applied with precision in every case. However, some method for arriving at a predetermined plan of radiation is essential for individualizing the treatment of each patient in the attempt to improve the results now obtained.

SUMMARY AND CONCLUSIONS

No single plan of radiation is suitable for all patients with cervical cancer. If the percentage of cures is to be increased materially, it is essential to individualize both the roentgen and radium treatment of each patient, rather than to apply a single method to all individuals.

Two important factors should be considered in planning the treatment of every patient: one, the minimum tissue dose necessary to control the lesion in question; and, two, the distribution of radiation throughout the tumor-bearing region. An intra-uterine tandem alone is inadequate for most patients with cervical cancer, due to the large dose falling upon the primary lesion and the relatively small amount arriving in the parametrial regions. The parametrial dose can be increased without administering excessive amounts from any particular source of radium if a greater number of sources are distributed throughout the tumor-bearing region.

Four patients in whom needles were employed in the treatment of primary or recurrent carcinoma of the cervix have been discussed. The location of the different sources used in each patient has been illustrated by means of radiographs made during the time radium was in place. A predetermined plan of radiation was worked out for each individual. The attempt was made to administer a tissue dose considered adequate for the lesion in question, and to deliver a distribution of radiation suited best to the volume of tissue to be treated.

There have been prepared for radium, isodose charts that can be used in the same manner as depth dose charts prepared by others have been used for x-rays. The method of preparing the charts has been described in detail. The isodose curves have proven to be useful aids in teaching the principles of interstitial radiation. They present a fairly rapid method for determining amounts of radiation required for delivering a predetermined tissue dose considered adequate for a given lesion. Furthermore, use of the charts necessitates a careful planning of radiation that insures individualization of treatment.

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ANALYSIS BY X-RAYS OF ULTIMATE STRUCTURES OF LIVING MATERIALS[1]

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SINCE the discovery in 1912 by von Laue and associates that crystals are three-dimensional diffraction gratings for x-rays, by virtue of the regular arrangement of the atoms and molecules upon lattice planes having spacings commensurate with x-ray wave lengths, a great chemical science of ultimate architectural structures of materials has risen to an eminent and well recognized place. Sir William H. Bragg and his son, Professor W. L. Bragg, began building upon the von Laue discovery and to this day retain their great leadership in the field. They demonstrated at once that a simple relationship governed the diffraction phenomenon and connected x-ray wave length, crystal interplanar spacing, and the angle of incidence, namely, the Bragg law

$$n\lambda = 2d \sin \theta$$

where n is an integer (the order of reflection), the x-ray wave length, d the spacing of a set of parallel planes in a crystalline substance, and θ the angle of incidence, or 2θ the angle of diffraction, of a pencil of rays.

Fig. 1. Laue pattern for single crystal of rock salt displaying cubic symmetry. By this same method in 1912 Laue discovered the diffraction of x-rays by crystals. Also, by this method a very narrow pencil ray, defined by pinholes, is transmitted through a stationary single crystal and the pattern registered on the photographic film at a fixed distance from the specimen.

In a comparatively short space of time hundreds of chemical compounds, inorganic and organic, metals, alloys, colloids, and materials of every imaginable variety have been subjected to x-ray diffraction analysis, with the result that indispensable information has been obtained upon what may be termed Nature's building plan, which is interpreted directly from the diffraction pattern. It is essential for such an interpretation, of course, that the material under investigation should have a spacial regular arrangement such as is readily inferred from a crystal of rock salt (Fig. 1) but scarcely from a cotton fiber or living nerve. And yet liquids and glasses, which are to be classed as amorphous in the usual sense, actually yield valuable data from the two or three broad halos which they produce as a pattern.

A reasonable and intriguing extension of the diffraction technic is, of course, to the great range of complex, highly polymerized materials which are formed in living processes. If it is found that these materials are sufficiently well organized in the sense of ordered arrangement of giant molecules, so that characteristic diffrac-

[1] Presented before the Fifth International Congress of Radiology in Chicago, Sept. 13–17, 1937.

tion patterns are produced, then it follows that x-rays may be expected to make a third great contribution to the field of medicine, in addition to diagnostic radiography and therapy, namely, a "supermicroscopic" analysis of biologically significant materials. It is the purpose of this paper to present very briefly an account of present knowledge of results on such materials. It will become immediately apparent that only the barest beginning has been made and yet the great promise of this application of x-rays is unmistakably indicated. An outline of the materials to be briefly considered as typical examples, and by no means a complete list, is as follows:

I. Cellulose
   1. Polymorphic forms: native, mercerized, Cellulose III
   2. Variations in orientation
   3. Regenerated cellulose
   4. Cellulose esters and compounds

II. Chitin
   1. Structure, orientation, reactions
   2. Chitosan

III. Rubber
   1. Structure on stretching
   2. Sol and gel
   3. Freezing and crystallization

IV. Proteins
   1. Fibrous
      (*a*) Silk fibroin
      (*b*) Hair keratin
      (*c*) Feather keratin
      (*d*) Gelatin and collagen
      (*e*) Muscle myosin
      (*f*) Living nerve
   2. Globular
      (*a*) Albumin
      (*b*) Hemoglobins
      (*c*) Insulin, pepsin, etc.
      (*d*) Crystallized virus.

I. Cellulose.—Cellulose forms the principal, and usually the crystalline, part of a large number of plants including ramie (Fig. 2), flax, jute, sisal, hem and cotton, wood, walls of the single-celled organism *valonia*, bacterial cellulose and tunicin, or animal cellulose. All these types of native cellulose possess the same fundamental structure, and differ only in respect to the relative orientations of cellulose crystallites and in the cementing and embedding materials. The giant molecules consist of a long chain of glucose residues ($C_6H_{10}O_5$) held together by 1–4 glucosidal oxygen bridges. The unit crystal cell is small and contains, of course, only a small number of the parent glucose residues, paired together as cellobiose. Thus, the length of the unit cell along the fiber axis, 10.3–10.4 Å., corresponds to the cellobiose unit, while the macromolecule extends through many such cells to a length corresponding to a molecular weight as high as a half-million. The accepted data on cellulose have been those of Meyer, Mark and Andress, as follows:

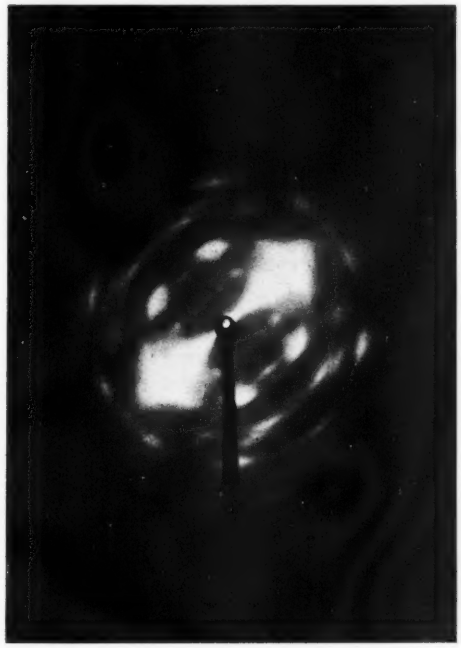


Fig. 2. Typical diffraction pattern for ramie, one of the natural cellulose fibers. Small bundles of the fibers are laid parallel and the x-ray beam transmitted perpendicular to the fiber axis. This pattern shows a high degree of crystallinity, all of the interferences being due to cellulose, and also a high degree of fibering or, in other words, a pronounced preferred orientation of cellulose crystallites with respect to the fiber axis. From such a pattern the complete crystal structure of cellulose is deduced.

a = 8.35 Å.U.
b = 10.3 (fiber axis)
c = 7.95
β = 78° (monoclinic system)
4 $C_6H_{10}O_5$ groups per unit cell.

By an analysis of intensities the parameters of carbon and oxygen atoms were determined and more recently corrected to give the most accurate picture of the cellobiose unit and the disposition along the edges and in the center of the unit cell. More recently, however, Sauter, by greatly improved technic, was able to register more than forty interferences which have not hitherto been observed on patterns, with the result that an entirely different interpretation is made, as follows:

a = 10.8 Å.U.
b = 10.4
c = 11.8
β = 85°
8 $C_6H_{10}O_5$ groups per unit cell.

This is in remarkable agreement with the original structure proposed by Sponsler and Dore, namely,

a = 10.7 Å.U.
b = 10.3
c = 12.2
β = 90° (orthorhombic).

An entirely different configuration of the chain is proposed so that the two glucose rings for cellobiose are not in the same plane.

Meyer and Mark presented the picture of rod-like cellulose micelles or crystallites about 300 Å.U. long and 50 Å.U. in cross-section, from a measurement of the breadths of diffraction interferences. Clark and Parker, by refined technic, studied the diffraction effects at very small angles, corresponding to very large spacings. There is a continuous series instead of sharp spots, running up to several hundred Å.U., laterally between cellulose chains or particles, suggesting considerable variability in these dimensions. Sauter has dismissed entirely a micellar or crystallite structure in favor of true long macromolecules ten times as long as the supposed micellar length of Meyer and Mark. The structure then consists of crystalline portions, amorphous interstices, and ultra-crystalline-fibrillar lattice splitting, to account for the highly complex physical and chemical behavior of cellulose. In 1934 the writer proposed that the ellipsoidal particles of cellulose, which appear when a pectin-like cementing material is chemically dissolved, with a constant length of 1.5μ and cross-section of 1.2μ, actually represented a bundle of chain molecules with a maximum length of 1.5μ. Such a chain would have a molecular weight of nearly a half-million in agreement with measurements by the ultra-centrifuge and by Staudinger's viscosity method.

Mercerized cellulose, prepared by treatment of native cellulose with alkali solutions followed by removal of all the alkali, is a polymorphic form of cellulose in which the chains are disposed differently with respect to the principal crystallographic directions in the unit cell and to each other. The monoclinic angle is considerably more acute (62°). This structure is consistent with observed characteristic properties such as ease of dyeing, greater absorbent properties, etc. Cellulose III is prepared by swelling native or mercerized cellulose in liquid ammonia, thus forming a complex ammonia-cellulose, followed by removal of the ammonia. Here the monoclinic angle is 58° and the interplanar spacings differ from those of the other two varieties.

Cellulose is characterized by a very long list of so-called topochemical reactions —the conversion of one crystal form into another in a fiber without destroying or indeed even seriously affecting the fiber in over-all structure or strength. Nitration, acetylation, reactions with alkalies, amines, etc., are all representative of important products which have been studied and identified by the x-ray method.

The various native cellulose fibers and sheets are distinguished by widely varying

types and degrees of preferred orientations of cellulose crystallites with respect to given directions. Quantitative measurements, experimental synthesis of all types of patterns, and correlation with physical properties have been presented by Dr. W. A. Sisson and the writer in a series of papers on natural and regenerated fibers and membranes.

II. Chitin.—Chitin is the compound that makes up most of the organic part of the skeletons of *Arthropoda*. In the animal kingdom, to which it is limited with very few exceptions, it occurs only in the invertebrates. In addition to forming the exoskeletons of insects, *Crustacea*, etc., it is the major constituent of the lenses of the eyes, the tendons, and the linings of the respiratory, excretory, and digestive systems.

Chitin is remarkably similar to cellulose in formation of long carbohydrate chains except that it contains nitrogen, thus moving a step toward the familiar proteins of the vertebrate world.

Chitin produces very rich fiber diffraction patterns from which is deduced the crystal structure[2] (Fig. 3). This is probably orthorhombic with the unit cell dimensions

a = 9.25 Å.U.
b = 10.46
c = 19.25.

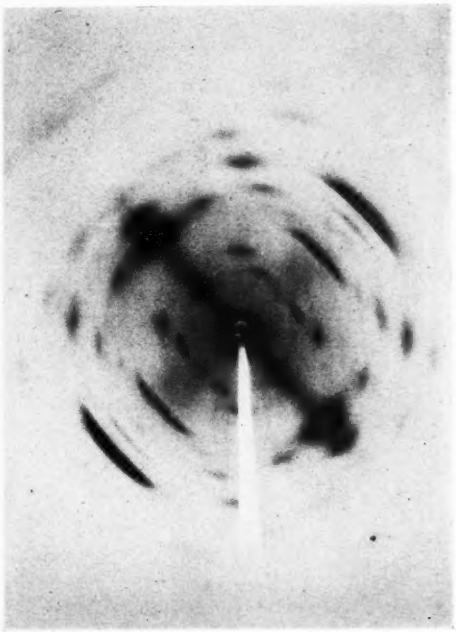


Fig. 3. Pattern for the mandibular tendon of a lobster composed of pure chitin. This substance is closely related to cellulose and it has a similar crystalline structure. However chitin contains nitrogen atoms. This is one of the most remarkably organized and crystalline of all natural materials. The shells of insects and the outer shell of lobsters and other crustaceans are composed of chitin as the organic part. The hard shells, of course, contain inorganic salts which can be removed by acid treatment. A very complete study of chitin and its chemical reactions has been published in the "Journal of Physical Chemistry."

As laid down in sheets, the only orientation is that the b axes are parallel to the surface. At a temperature of 200° C. chitin forms a definite addition compound with lithium thiocyanate, while at lower temperatures intramicellar swelling occurs. Various fractions of chitin nitrate have different average lengths of the carbohydrate chain. Chitin nitrate is orthorhombic with

a = 9.2 Å.U.
b = 10.3
c = 23.0.

A whole series of compounds is formed with sodium hydroxide, but it is difficult to isolate pure compounds and to obtain sharp patterns because of hydrolysis.

Chitosan is the compound formed by hydrolysis of half the acetyl groups in chitin. When formed from a sheet, it undergoes a change to a more restricted orientation such that the 002 planes become parallel to the surface of the sheet. The unit cell of chitosan (monoclinic) has the dimensions

a = 8.9 Å.U.
b = 10.25
c = 17.0
β = 88°.

Like chitin, chitosan forms a long series of interesting addition compounds with distinctive patterns. While chitin gives a con-

[2] Clark and Smith, Jour. Physical Chem., 1937, **40**, 863.

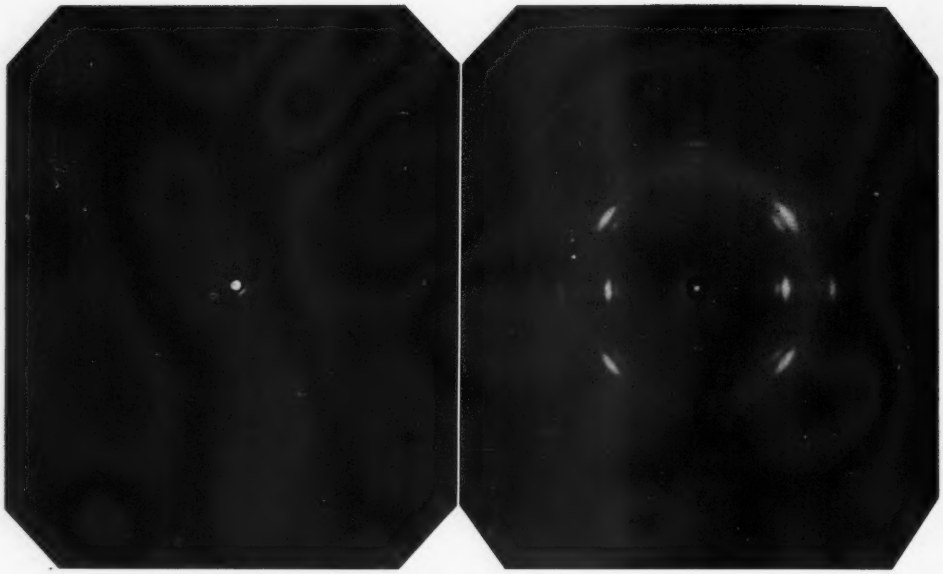


Fig. 4. Patterns for unstretched rubber and the same rubber stretched 500 per cent. The former pattern is characteristic of a liquid or glass with a single broad halo. When rubber is stretched, long tangled molecules are apparently pulled into parallel alignment and crystallization and fibering are the result. From such a pattern a great contribution has been made to the knowledge of the structure of rubber. Rubber may be separated into two fractions, ether-insoluble or gel rubber, and ether-soluble or sol rubber. Only the total or gel rubber produces a pattern of this kind upon stretching, while sol rubber does not, even at 1,000 per cent elongation. Also, gel rubber produces a long spacing close to the center of 54 Ångström units, which is completely missing in sol rubber.

tinuous series of long equatorial spacings like cellulose, chitosan produces resolved maxima in several orders corresponding to a definite lateral spacing between molecular chains or crystallites of 7.5 Å.U. This spacing increases markedly upon swelling in dilute alkali.

III. Rubber.—As an example of coagulated latex produced by numerous plants, we may select rubber (*Hevea brasiliensis*). X-rays have made a notable contribution to the knowledge of this remarkable substance. Ordinary unstretched rubber produces a pattern characterized by two or three broad halos exactly as a liquid or glass. Instantly upon stretching, however, a rich crystal fiber pattern is obtained which has led to an evaluation of the structure of these polymerized C_5H_8 chains (Fig. 4). The fibering appears only beyond a critical elongation which depends upon the state of the specimen, vulcanization, temperature, solvent, or fractionation. The approved data[3] for the monoclinic unit cell are as follows:

$$\begin{aligned} a &= 8.54 \text{ Å.U.} \\ b &= 8.20 \\ c &= 12.15 \\ \beta &= 83^\circ 20'. \end{aligned}$$

Space group C_{2h}^5, four principal valence chains for cell

$$8\ C_5H_8.$$

The long chains have a two-fold screw axis of symmetry. The actual crystallite is a molecular racemate of right- and left-handed spiral molecules.

Comprehensive work has been done on the ether-soluble (sol) and ether-insoluble (gel) phases of rubber in the writer's laboratory. Sol rubber will not produce a fiber pattern even upon stretching above 1,000 per cent, while gel rubber (and, of

[3] Lotmar and Meyer, Monatshefte für Chemie, 1936, **69**, 115. Clark, Wolthuis, and Smith, National Bureau of Standards Jour. of Research, 1937, **19**, 1039.

course, total rubber) is responsible for the fiber pattern upon stretching. The latter, furthermore, has a characteristic long-spacing of 54 Å.U. (or a multiple) which is completely lacking in sol rubber. Sol rubber, upon vulcanization, can be made to produce a fiber pattern as a further confirmation of the concept that sulphur forms stiffening cross-linkages between long backbone molecules.

When rubber is kept cold for a long time it becomes opaque and the "amorphous" halo pattern gives way to a sharp line pattern characteristic of a powder. An analysis in the writer's laboratory proves that these true crystals possess essentially the structure already derived from the fiber pattern produced on stretching. Identical with these patterns are those for *pure sol and gel crystals* produced at the National Bureau of Standards.

Gutta-percha, balata, and chicle have also the general formula $(C_5H_8)_n$ but differ widely from rubber. They are crystalline at ordinary temperatures without stretching, and undergo a polymorphic transition to a new molecular configuration at 65°. In the fully extended rubber chain the molecular groups are in *cis* position, while in gutta-percha these are in *trans* position.

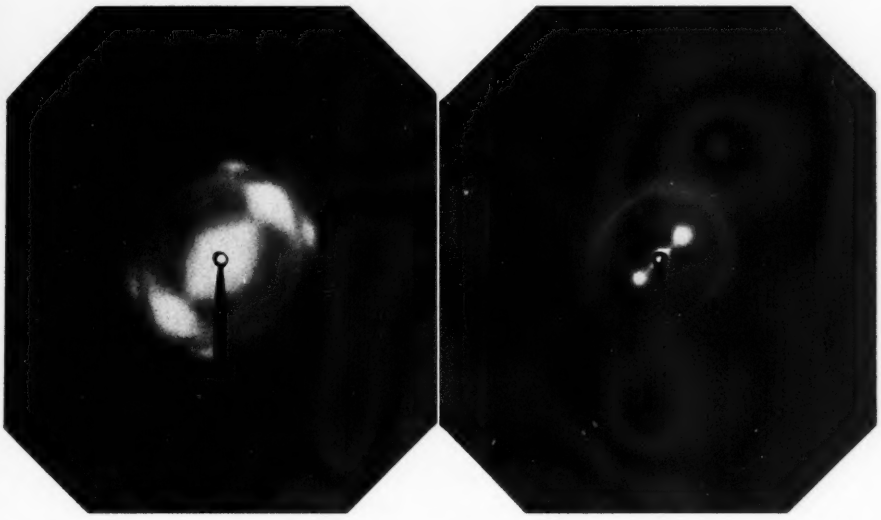


Fig. 5 (*left*). Pattern for natural silk—a protein called "fibroin" synthesized by the silk worm. Cobwebs give an entirely similar pattern.

Fig. 6 (*right*). Pattern for human hair or keratin. When hair is stretched this pattern changes completely into a new molecular configuration, which accounts for many of the peculiar properties of hair and wool.

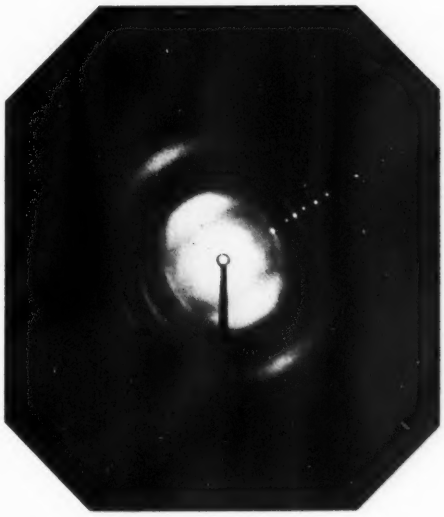
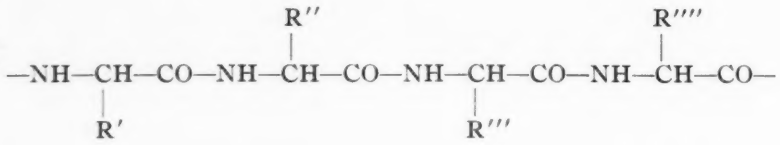


Fig. 7. Pattern of the feather of a bird. Also keratin but decidedly more crystalline and differently oriented.

Mack[4] has proposed the most comprehensive theory of these differences and of the mechanism of elastic stretching, called a hydrogen evaporation-condensation mechanism. Of all synthetic rubber specimens, only chloroprene has yielded a fiber diffraction pattern upon stretching similar, but not identical with, that of rubber.

IV. Proteins.—Since the beginning of this century and as a result of the work of Emil Fischer and others, proteins have been considered to be long chains formed from repeat condensations of α-amino acid ($NH_2—CH(R)—COOH$) to a configuration of the type



Thus a more or less common backbone is characteristic of all fibrous protein molecules and differences arise from the nature of the side-chains or R groups.

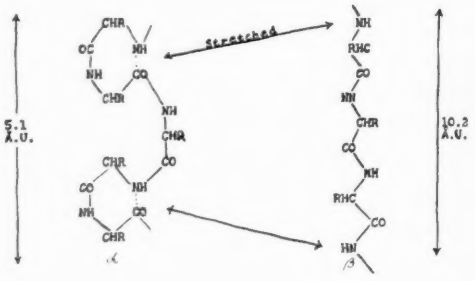
Silk Fibroin.—Silk fibroin, a natural crystal fiber, is distinguished by stability and simplicity since it yields, on hydrolysis, principally glycine and alanine. Thus its R groups are only hydrogen and CH_3. The x-ray pattern is fully consistent with the above concept of a fully extended polypeptide chain (Fig. 5). The unit monoclinic cell has the dimensions

a = 9.68
b = 7.00 (2 amino-acid residues of 3.5 Å.U.)
c = 8.80
β = 75°51′.

Stretching has no effect on the pattern; hence, the crystallites being already stretched to the fullest extent, merely slide over one another.

[4] Mack, Jour. Am. Chem. Soc., 1934, **56**, 2257.

Keratin (Mammalian Hair).—To Astbury is due the present extensive knowledge of keratin, or the protein of hair, wool, horn, etc. When stretched, these produce patterns of β-keratin similar to silk fibroin; but in the normal unstretched state, a completely different pattern for α-keratin indicates some regularly folded condition of the backbone of the molecule from which it may be pulled out straight in the presence of moisture and to which it returns upon release of tension (Fig. 6). Thus the molecular configurations of the normal and stretched hair may be represented as follows (see figure below):



The β-keratin then forms a grid, built up by interactions and combinations between the R groups of neighboring main chains. The crystal particle consists of a series of parallel grids. The dimensions roughly are

Amino-acid residue along main-chain	3.5 Å.U.
Side-chain spacing	10.0 Å.U.
Spacing between grids	4.5 Å.U.

This form may be set permanently when the hair is steamed in the stretched state, simply because cross-linkages are hydro-

lyzed and reformed in a configuration which will prevent return to the folded α-state. The α-form has the main-chains folded so that the grids are buckled. Now wool and hair can be treated by steam or alkali in the extended state so that upon release they exhibit supercontraction to a length shorter than normal. Thus the α-folding is still further elaborated to about one-third the length of β-keratin and must be due to fundamental changes in the cross-linkages of the grid as demonstrated actually on the x-ray patterns.

Feather keratin produces a remarkably rich pattern which is based fundamentally on the simple α-and β-keratin structures and pattern, but greatly elaborated and actually approaching some of the crystallized proteins (Fig. 7).

Muscle.—All of the above observations on diffraction patterns, structure, behavior on stretching and supercontraction in keratin have now been duplicated by Astbury for the protein in muscle, namely, myosin. The photograph of washed and dried muscle, and indeed of living muscle, if the presence of water is taken into account, is remarkably like that of α-keratin; that of stretched myosin is also like that of β-keratin. Hence, myosin possesses folded chains in the condition at rest, which are further folded upon supercontraction. Since keratin possesses a much higher sulfur content from its cystine constituent, the side linkages between neighboring chains may be through the —S—S— groups, so that a hair may be considered as a "vulcanized" muscle fiber with reduced elastic sensitivity and increased resistance to chemical attack.

Collagen.—The principal constituent of vertebrate tendons and tissues is the protein collagen, which, upon hydrolysis, yields gelatin. Surgical catgut ligatures are collagen fibrils from the intestinal walls of sheep. An extended x-ray study of catgut in the writer's laboratory has led to greatly improved processing of the ligatures in the sense of uniformity and enhanced tensile strength. This was achieved largely through improved preferred orientation of protein crystallites under combined swelling and tension.[5]

Collagen and gelatin, being made up of fifteen or more amino acids of widely different functional groups and molecular weights have previously not given patterns with sufficient orientation and number of interferences to lend themselves readily to analysis. Long-chain molecules are rather easily oriented by tension but lack sufficient organization of amino acid residues to produce a well-defined lattice. The existence of a halo, which shows indication of partial orientation, superimposed upon a faintly sharp interference pattern indicates a "pseudo-crystalline" structure. On the pattern appears inner equatorial arcs for a spacing of from 10.4 to 17.0 Å.U., depending on the amount of water held by the protein and measuring the distance between main chains, or the length of cross-linkages; a spacing of 4.5–6.1 Å.U. corresponding to the thickness of the grid; and a fiber axis identity period of 9.75 Å.U., or three times an amino-acid residue length of 3.25 Å.U. Another spacing of 2.84 Å.U., thought by Astbury to be a contracted residue length, is due to planes which are not perpendicular to the fiber axis. Both collagen and stretched gelatin ribbons give essentially this same type of ordinary pattern.

Clark, Parker, Schaad, and Warren[6] first reported the existence of a spacing along the fiber axis in collagen of 432 Å.U. (the longest ever directly measured) which is completely missing in gelatin. This gives a remarkable clue to the organization of collagen in contrast with gelatin. This spacing indicates a regularly repeating residue along the chains or an over-all length of the molecules themselves. In addition, a lateral equatorial spacing of 48 Å.U. is noted for intestinal wall but not for tendon collagen. The orthorhombic unit cell of the addition compound amino-

[5] The X-ray in the Study of the Catgut Ligature, G. L. Clark and P. F. Ziegler, Surgery, Gynecology and Obstetrics, **58**, 578; Surgical Ligatures, Clark, Flege, and Ziegler, Ind. Eng. Chem., **26**, 440.

[6] Jour. Am. Chem. Soc., 1935, **57**, 1509.

acid residue: NaOH = 1:1, has the dimensions

a = 5.32 Å.U.
b = 6.50
c = 11.90
2 residues per cell
Density = 1.372
Calculated molecular weight = 170.

This reaction is reversible since the original collagen pattern is regained after treatment of the alkali addition compound in a buffered solution at the iso-electric point *p*H 4.78. Addition compounds with entirely different structures and patterns are formed with KOH, LiOH, RbOH, and CsOH. The spacing 432 Å.U. decreases to 408 Å.U. for chromicized gut without further evidence of inter-action of the chromicizing solution with collagen.

The peculiar behavior of the 48 Å.U. interferences on treatment of the fibers with hot water, alkali solution, salts, and various organic solvents led to the discovery by Clark and Schaad of a wax-like substance whose molecules are radially oriented on collagen fibrils in these wall tissues and serve both as a lubricant and as a protection against enzyme digestion of the collagen. Analysis indicates an empirical formula of $C_{14}H_{28}O_2$ or a multiple and that the compound may be related to cholesterol derivatives rather than an ordinary ester. It is evident that this substance, which is completely absent in tendon, is synthesized or adapted by the body for this very specific purpose. The power of the x-ray diffraction method in biological research is clearly indicated by this example.

Nerve.—The diffraction patterns of fresh and dried medullated and non-medullated nerves are described in a paper by Schmitt, Bear, and Clark.[7] Medullated nerves are represented by the sciatic, motor, and sensory roots of the frog and cat and by the corpus callosum of the cat; non-medullated nerves by the claw and leg nerves of the lobster and crab.

The pattern of fresh medullated nerve is probably due entirely to oriented fluid crystals of the myelin sheath, for it can be reproduced fairly completely in preparations made by rubbing up a benzene extract of spinal cord with water. The fundamental aggregate of these fluid crystals appears to have dimensions of $4.7 \times 9.4 \times 171$ Å., the various lipoids being associated in a mixed crystal fashion. The *c* spacing lies radial and perpendicular to the long direction of the axon. This means that in thinly myelinated fibers the myelin sheath is composed of but relatively few layers of these oriented lipoids associated end to end.

With the exception of the equatorial sickles at 11.5 Å., the patterns of dried medullated nerve can be reproduced by dried extracted lipoids. Rings with spacings characteristic of phosphatids and of cholesterol can be identified in the pattern of dried nerve. Drying disorients certain of the components of the myelin, leaving others fairly well oriented.

Heating frog sciatics causes a disorientation of the lipoids which appears to occur at or about the same temperature at which the action potential is extinguished. Higher temperatures, which cause maximal shortening, have little further effect on the x-ray patterns.

Patterns of frog sciatics treated with cyanide until the action potential was blocked departed little from the normal.

To study the structure of the axis cylinder, lobster and crab leg and claw nerves were used. These nerves have in the past been assumed to represent pure axis cylinder, containing little or no connective tissue or lipoids. This assumption has been shown to be incorrect by chemical analysis and by histologic investigation. The lipoid content may be as high as from 25 to 30 per cent of that of the white matter of mammalian brain. Connective tissue is by no means negligible; there is interfibrillary connective tissue as well as fibrous material closely adherent to each fiber. There is also a sheath which appears to be comparable to the Schwann sheath. These facts greatly complicate the analysis of the axis cylinder since the proteins of the axis

[7] RADIOLOGY, 1935, **25**, 131.

cylinder give spacings similar to those of collagen of the connective tissue.

Artificial fibers spun from the nucleo-proteins of lobster nerves, though positively birefringent, indicate no orientation in their diffraction patterns. A ring of 9.1–11.5 Å. represents the proteins. Even though these fibers were spun from fat-extracted protein, rings at 48, 23, and 4.8 Å. represent the lipoid components.

Alcohol-dried lobster nerves show equatorial sickles at approximately the same spacing as that given by the nucleo-protein of the axis cylinder. This fact was originally interpreted as showing that the axis cylinder contains oriented protein micelles. This conclusion must be qualified in view of the demonstrated presence in these nerves of collagenous material which might be responsible for at least a part of the orientation.

Although lipoids are present in very appreciable quantities in lobster nerve, they give rise to no pattern in fresh nerve. However, if the nerve be treated with glycerine, which changes the birefringence from positive to negative, patterns may be obtained which demonstrate that the lipoids have become oriented. Preliminary experiments indicate that cholesterol and perhaps also the phosphatides are involved in the effect.

The nerve of the squid represents the nearest approach to a pure giant axon yet found. This material, though displaying weak birefringence, presents an essentially amorphous pattern. It is estimated that only about 8 per cent of the long-chain protein molecules in the axis cylinder are actually in any preferred orientation.

Globular Crystalline Proteins.—The obvious limit of the idea of folding and twisting protein chains is to be found in the so-called globular proteins such as egg albumin, hemoglobin, edestin, etc. These substances may actually be crystallized in a sense far different from the fibers just discussed. It would appear that they are built in a very delicately balanced fashion of somewhat spherical units which have been shown so brilliantly in the work of Svedberg with the ultra-centrifuge, to have molecular weights of 35,000 or a multiple. X-ray work by Bernal and Crowfoot[8] on pepsin and insulin crystals have definitely confirmed this contention. Clark and Shenk[9] have made an extensive study of crystallized and denatured egg albumin. In the usual case the patterns for these proteins consist essentially of two halos corresponding to the two principal distances between main chains, 10 and 4.5 Å.U. By boiling and other methods of denaturation, the pattern resembles even more strongly that of powdered or disoriented β-keratin, showing that a highly specific and delicately balanced configuration in the original globular protein is broken down. By stretching, Astbury has succeeded in orienting denatured albumins and globulins so that fiber patterns are produced. Thus denaturation actually liberates polypeptide chains from crystalline proteins and permits their conversion into visible fibers which, on stretching, are found to be structurally analogous to stretched wool and unstretched silk.

Clark and Shenk[10] have shown that denatured hemoglobins give diffraction patterns very similar to those of egg albumin. X-ray studies are made of rat and horse oxyhemoglobin and horse and pig carbon monoxide hemoglobin. The two horse hemoglobins with a maximum spacing of 48.2 Å.U. seem to be the same, but the patterns for blood from different animals are not alike. The color constituent of hemoglobin, hemin, chlorohemin, potassium oxyhemin, and other derivatives are all identical from all sources.

Of greatest recent interest has been the x-ray analysis of crystallized tobacco mosaic virus protein, isolated first by Dr. W. M. Stanley, of the Rockefeller Institute for Medical Research. The significance lies in the attempt to explain how this material, placed in the proper environment, is able to produce more of itself, and whether, or how closely, a crystalline protein comes to

[8] Nature, 1934, **133**, 794; 1935, **135**, 591.
[9] RADIOLOGY, 1937, **28**, 58.
[10] RADIOLOGY, 1937, **28**, 144.

the process of life. Wyckoff and Corey,[11] Bernal and associates,[12] and Clark and Parker have all studied this virus. Bernal has found a maximum spacing of 152 Å.U. for the dry gel, 210 for the wet gel (hexagonal close-packed), and 300–470 for liquid preparations. A second interference appears at 75–80 Å.U., which has been found by the other workers also. More than twenty interferences appear on some patterns. Further progress will be awaited with greatest interest.

Reaction of Formaldehyde on Proteins.—Clark and Shenk[13] have shown that proteins such as gelatin, egg albumin, and hemoglobin, after treatment with formaldehyde, give diffraction patterns containing two rings of amazingly great intensity, neither of which appears in the pattern of the original protein. Casein, zein, and fibered proteins, *except* silk *fibroin*, act similarly after a brief preliminary swelling in dilute alkali. The two new spacings, 3.9 Å.U. and 2.6 Å.U., are due, respectively, to a slightly extended amino-acid residue, and to a second order of an increased backbone spacing. A very powerful reaction, probably on amide nitrogens, has probably tied two adjacent chains together. This remarkable effect suggests a whole series of reactions on proteins. It is of significance since the formaldehyde treatment hardens plastic proteins, and is the basis of manufacturing processes.

Monomolecular Films of Proteins.—Langmuir, Schaeffer, and Wrinch[14] have developed the method by which many proteins capable of existing in water as large spherical molecules can be spread on water surfaces giving elastic solid monomolecular films having great two-dimensional compressibility. Such mono films may be transferred from a water surface onto solid surfaces, whereby counting the total number of layers may be determined and the thickness measured by optical or x-ray methods. This work has demonstrated that if films are transferred to a solid backing by pushing into the water and then pulling out the plate, one surface of the protein film is predominantly hydrophilic. A careful study of all the properties of these films has led these workers to the view that the protein mono layer is a two-dimensional network held together by strong elastic springs and is not in accord with a structure consisting of polypeptide chains. X-ray studies have just been undertaken in the writer's laboratory upon multiple films. When a thickness exceeding ten layers is used there is quite unexpectedly distinct evidence with egg albumin from sharp interferences in several orders of a spacing of 73.3 Å.U., but the characteristic 10 Å.U. spacing which represents the length of the side spacings, and one of about 4.5 Å.U. for the backbone spacing or the thickness of grids are not detected. Added interest in the whole problem, which still requires much experimental work, is based upon the theory proposed by Dr. D. M. Wrinch of a further elaboration of the folding of protein chains into a cyclol pattern. This gives to a protein sheet a framework upon which may be superposed a large number of physiologically active compounds, including the carcinogens, sterols, bile acids, sex hormones, and heart poisons. The cyclol pattern depends upon the assumption, namely, that amino-acids can condense by means of single, double, or triple peptide links. When such a cyclol pattern is formed, all the side chains emerge from one surface whereas the other surface is free from side chains. Hence, it is possible for proteins with the most diverse chemical composition to share one common surface pattern, namely, that on the surface free from side chains. The extension of this concept of the use of large molecules of various types, including proteins, as templates is exceptionally promising as an interpretation of many biological mechanisms. The theory is now being subjected to careful x-ray analysis.

[11] Jour. Biol. Chem., 1936, **116**, 51.
[12] Nature, 1936, **138**, 1051.
[13] RADIOLOGY, 1937, **28**, 357.
[14] Science, 1937, **85**, 76.

THE EVOLUTION OF RADIOTHERAPY, DURING THE PAST TEN YEARS, IN THE TREATMENT OF CERTAIN GENERALIZED AFFECTIONS[1]

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Translation by A. U. DESJARDINS, M.D., *The Mayo Clinic, Rochester, Minn.*

I THANK the organizing Committee of the Congress, and especially our Section Chairman, Dr. Desjardins, for the honor of having been selected as honorary chairman of this session.

The radiologists of Europe have the privilege of meeting this year in a country which offers them perspectives which are very original and full of instruction. Thanks to our congresses, we come to know not only the ways and methods of work of each ethnic group, but also the men and the spirit which animates them. We congratulate ourselves on being in the midst of our American colleagues and on being able to approach the radiologic élite of the New World.

These congresses also enable us to obtain our bearings in certain controversial questions. This is why it seemed worth while to open this session by seeking what new developments the methods of irradiation have brought us during the past ten years; that is, since the appearance of total teleroentgentherapy.

In order to keep within the time limit, I have chosen chronic leukemia, essential erythremia, and malignant granulomatosis. I do not pretend to bring you decisive ideas. I intend merely to express an opinion concerning a complex problem which we are not yet in position to solve.

Before 1927, except for experiments on animals and for an early, technical rather than clinical attempt by Dessauer, the classic method of applying radiotherapy consisted in local, segmental irradiation of the human body, whether one was dealing with circumscribed lesions or with a generalized affection.

Even during the early days of radiotherapy, leukemia and granulomatosis (Hodgkin's) were classed among the very radiosensitive conditions; the new method, which constituted a great progress, gradually imposed itself; it became the dominant treatment of these frightful diseases, without, however, being able to claim rank as a curative agent.

Might we find, thanks to improvements in technic and to more powerful apparatus, a more rational method which, in conditions so widely disseminated through the body, might serve to improve the results of this palliative agent? The idea of irradiating the entire body in a single field was tempting. Werner Teschendorf, as well as Dale, deserves the credit of having opened new horizons by different paths.

The method and the results of segmental radiotherapy are familiar to us all; I need not recall them to you.

What objections have been raised against the classic method? Against it has been held the inability of prolonging life in these diseases. It yields remissions of excellent quality, but death supervenes in the same time, whether the patient has been irradiated or not. At least, this is true in the leukemias, as has been shown by Minot (1924) and Hoffman and Craver (1931). As for malignant granulomatosis (Hodgkin's disease), the case is different. The idea advanced in 1924 by Klewitz and Lullies, and by many other authors, is no longer warranted if the method of irradiation is correct: the majority of cases present more definite and longer remissions and life is incontestably prolonged. I have submitted proof of this at the General Session; I shall not repeat it now.

[1] Presented before the Fifth International Congress of Radiology, in Chicago, Sept. 13–17, 1937.

LEUKEMIA

As for leukemia, Naegeli, of Zurich, contends that if arsenical medication is combined with radiotherapy, the result is to delay the appearance of an increasing resistance to irradiation, which paralyzes further action. An investigation conducted in the services of Naegeli and Schinz seems to support this assertion.

In order to keep in reserve an agent as valuable as radiotherapy, says Naegeli, one should first employ an intensive treatment with an arsenical preparation, parenterally as well as by mouth. And once roentgen therapy has been started, one should avoid repeating it too frequently. What should be the criterion? Doubtless the condition of the blood, but the therapeutic radiologist must not allow himself to be impressed too much by a mere increase in the number of leukocytes; if the patient feels well, if his general condition is good, if he has little or no anemia, if his blood does not contain too many immature cells (especially myeloblasts), the treatment should be postponed, even when the leukocytes reach 50,000 or 100,000 per cubic millimeter. Delherm and Stuhl, as well as others of us, have made similar observations. It follows that it is easier to stop the treatment according to the behavior of the blood than it is to know at what moment the treatment should be resumed. Here, it would seem, we have a means of deferring the appearance of radioresistance and, at the same time, of extending the limits of efficacy of the classic treatment.

It was precisely the myeloses which had become refractory to treatment which impelled Teschendorf to try irradiation of the entire body at a long focal distance.

The structures which give birth to the blood corpuscles—bone marrow, lymphoid organs, reticulo-endothelial tissue—are widely scattered in the body. Hence, the idea that by simultaneous irradiation of all the pathologic foci the results of radiotherapy would be improved. However, it is noteworthy that such a distribution of foci, by itself, does not explain the failures of segmental irradiation since, in the myeloses, irradiation of the spleen alone often yields a primary remission which is remarkable by its quality and by its duration. The intimate mode of action escapes us.

On the other hand, it may be considered as established that once a leukemic patient has become resistant to the classic method of irradiation, he may still be capable of responding favorably to teleroentgentherapy of the entire body.

I do not intend to confine myself to the physical data and to the method of utilizing panteleroentgentherapy as expounded by W. Teschendorf, by Dale, by Cottenot and Sluys, by Mallet, Marshall, Sgalitzer, Ducuing, Marques, and others, and studied from another angle by Palmieri and by the late Heublein.

I shall examine the clinical results, then the disadvantages of panteleroentgentherapy in the conditions mentioned.

The results obtained by Teschendorf in myeloses which had become refractory to treatment, led him to adopt panteleroentgentherapy as the method of choice in this variety of leukemia, His method of irradiation is as follows: (1) as a treatment of attack; (2) as a continuing treatment to maintain the improvement obtained and to prevent recurrence. He observed that, in contrast to the classic method of treatment, panteleroentgentherapy must be continued periodically (about every two weeks), otherwise the disease is prone to recur. Is life really prolonged? This does not emerge from his report (1) of 1937, although some authors have claimed that the results are shown by a better quality and a longer duration of the remissions.

In lymphoid leukemia, Cottenot and Sluys have obtained remarkable results, while Teschendorf and Sgalitzer are more reserved; the two latter prefer a combination of segmental irradiation and total teleroentgentherapy. In such cases they all recommend the greatest prudence, because very small doses (15 r) repeated within too short a time caused a startling

decrease in the leukocytes, erythrocytes, and hemoglobin in one case (as much as 600 leukocytes per cubic millimeter, a million erythrocytes and 20 per cent in the hemoglobin). Cottenot and Sluys write: "Everything takes place as if the massive destruction of lymphocytes in the tissues and in the blood liberated toxins capable of destroying erythrocytes."

ERYTHREMIA

Erythremia (synonyms—Vaquez' disease, essential polyerythrocythemia, polycythemia rubra) deserves special consideration. When irradiation of the spleen had been shown to exert only a mediocre influence, my colleague, Lüdin, of Basel, was the first to demonstrate the necessity of irradiating the bone marrow. This mode of irradiation by innumerable small fields yielded brilliant successes, but it had the disadvantage of being tedious and costly, and was not always successful. As early as 1928, Sgalitzer applied total teleroentgentherapy to this disease. In 1937 he reported that of 44 irradiated cases, 42 had responded favorably to teleroentgentherapy, many of them having proved refractory to segmental irradiation of the bone marrow. The results are frankly encouraging. As in leukemia, there is no cure, but recurrence appears to be the more delayed as the first series of irradiations has been more thorough. The number of erythrocytes should be reduced progressively to 4,000,000, without the leukocytes ever falling below 3,000. This depends on the dose at each session and on the rhythm of irradiation. Several authors have confirmed these results.

At the present time, Sgalitzer concludes that, if total teleroentgentherapy as compared with segmental irradiation constitutes a remarkable progress in the treatment of leukemia, the results which it yields in erythremia are even superior.

Quite different are the results of this method in malignant granuloma (Hodgkin's disease). In this condition panteleroentgentherapy produces such strong general reactions that the protagonist of the method, Teschendorf himself, has given it up. He prefers roentgentherapy of the entire trunk through large and separate fields (Sluys), combined with local irradiation of the tumors. Personally, I am opposed to panteleroentgentherapy for granulomatosis, for the reasons given in my report (2). Belot and Sgalitzer, who have tried it, have abandoned it. Belot (1935) expressed strong doubt that the small doses absorbed at the level of the granulomatous foci are sufficient to destroy the affected tissues: experience has taught him that, in order to obtain a result, the sessions must be repeated and the total dose, in the majority of cases, must be large enough to jeopardize the general condition of the patient and the blood formula. While irradiating large mediastinal tumors, Ponthus and Piante observed an improvement in general condition, but the local effect was mediocre; however, on subjecting the mediastinum to classic segmental roentgen therapy, they saw the tumors melt.

On the contrary, Marchal, Mallet, Cottenot, and Lemoine, who irradiated cases of leukemia and of Hodgkin's disease, declared in 1934 that their former optimism in respect of the leukemias had moderated, while in granulomatosis their results were distinctly superior to those of the previous year. They have treated 18 cases during different phases of the disease, and they report that half of the cases are in a state of apparent cure, but only five of these nine cases were treated with total teleroentgentherapy alone; all the others had also received local roentgen therapy; this, however, falls within the conception of the authors. In view of the small number of cases, the short period of observation, the contradictory results of other authors, I can only record the facts and wait until the partisans of the method are in position to report results comparable with those of segmental roentgen therapy which, in granulomatosis, has proved its worth.

I have alluded to another method of irradiating the entire body, that of Sluys. This consists in irradiating in succession

large, overlapping fields (one field each day), the body being divided into from four to seven ventral fields, and as many dorsal fields. It does not present the dangers of panteleroentgentherapy, and makes it possible to give, in malignant granuloma, doses of 250 r every day or every other day, or a total dose of 1,000 r per field. Until now, it has been little used in the conditions with which we are dealing: I mention it only as a matter of record.

An interesting fact; when one is dealing with a condition characterized by slight or pronounced tumefaction of lymph nodes, panteleroentgentherapy alone usually does not suffice to make them disappear—not permanently, at any rate; while segmental irradiation, with its concentration of dosage on a smaller volume of tissue and, therefore, with its direct destruction of cells, achieves this effect without any damage to the general condition of the patient.

It is easy to understand, therefore, why the advocates of panteleroentgentherapy or of total irradiation by segments should also favor local irradiation whenever total irradiation does not bring about the expected local modifications: the two methods do not exclude each other; rather, they complement each other.

In fact, nothing in panteleroentgentherapy could be more dangerous than to increase the dose given at each session or to repeat the sessions too frequently, simply because a spleen or a mass of enlarged nodes does not diminish in volume. This method requires exact dosage and extreme prudence in the rhythm of irradiation. In truth, the minimal size of the doses is only apparent, because, while the dose per unit of surface is small, the total energy absorbed is very great (this is what the German authors refer to as *Raumdosis*). Moreover, beside the question of dosage, there exists "an extremely complex series of biologic factors which, together, constitute individual tolerance" (Marchal and his coworkers). As the usual dose per session, Teschendorf mentions 6 to 15 r only, of which one-half is given to the ventral surface and the other half to the dorsal surface. In myeloid leukemia the dose is repeated only after an interval of from eight to fifteen days, according to the numerical behavior of the leukocytes. In erythremia Sgalitzer begins by "test irradiations" for six consecutive days, alternately through the ventral and dorsal surfaces, with a maximal dose of 1/25 H.E.D., or less than 25 r (Teschendorf mentions a dose of from 5 to 7 r); this trial is followed by a blood count, not for the erythrocytes which would not have had time to diminish, but to watch the leukocytes which vary so much in different patients according to their individual susceptibility to irradiation. This fact, to which Cottenot and Sluys have drawn attention, led Sgalitzer, in erythremia, to extend the cycle of irradiation over a period of four weeks (a total of from 12 to 22 sessions, with repeated blood count) when the leukocytes prove resistant, while the cycle is extended over a period of two or two and a half months when the leukocytes prove too sensitive to this mode of irradiation.

This makes the dangers of the method quite obvious. Experimental investigations had led us to suspect these dangers, and during the past few years these suspicions have been confirmed. I shall consider especially the hematologic accidents observed by different authors. Except the startling but rather inconstant decreases in the number of leukocytes which have already been mentioned, analogous decreases of the erythrocytes, as well as thrombopenia with its grave complications may occasionally be observed after a certain latent period. A late and progressive anemia may sometimes correct itself or may be repaired by repeated transfusions. The fact that in 1934 Marchal and his co-workers advised immediate interruption of total irradiation when the erythrocytes fall to three millions, or when a sudden, sharp fall of the erythrocytes (for example, from 5,000,000 to 3,800,000 in one week) impresses one with the risk involved. According to Marchal and Mallet, the fall in the erythrocytes is due to the fact that total teleroentgentherapy

acts in only one direction on the hematopoietic system—therefore, without compensatory reactions of the blood-forming organs— while the latter are spared by segmental irradiation. Owing to the risk of severe anemia, Aubertin (1936) justly advised great prudence in the use of panteleroentgentherapy.

The mode of action of total teleroentgentherapy remains obscure; I shall avoid discussing it. The problems which it raises exceed the scope of the conditions considered; it relates also to certain diseases of the skin, of the endocrine glands, as well as cancer. In 1936 Desplats again stressed the hypothesis of an indirect, functional or humoral action, while Teschendorf wrote of the "*Umstimmung des Körpers.*"

SUMMARY

The clinical results of panteleroentgentherapy in leukemia, erythremia, and granulomatosis are contradictory and unequal from one condition to the other. At the present time, the best results are obtained in leukemia (especially in the myeloid forms), and especially in erythremia. Save in this last condition, the relatively few things which are known do not warrant, in my opinion, the abandon of the classic method, but it would seem that total teleroentgentherapy and local, segmental, roentgen irradiation should complement and support each other. It cannot be denied that total teleroentgentherapy has proved efficacious when segmental irradiation had exhausted its effect; I have demonstrated this myself in leukemia and in one case of erythremia.

If the usefulness and opportuneness of the method are still much debated, this is because of its real danger and its uncertainty. It is essential to know the risks well and to give constant attention to the question of individual tolerance, because of its unforeseeable variations.

I should like to express a wish: it is that the papers read in this section (of the Congress) may bring us new light, not only on the method, its indications and contraindications, but also on the interesting biologic problems which it raises.

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(2) GILBERT, R.: Le traitement de la granulomatose maligne; bases anatomo-cliniques; principes directeurs; résultats. Rapport au V^e^ Congres International de Radiologie, Chicago, 1937.

COLON SPASM

By HORACE W. SOPER, M.D., *St. Louis, Mo.*

THE clinical significance of spasm of the colon has not as yet been clearly established. The spastic colon and its relationship to constipation is generally recognized. Errors in diagnosis are frequently made in spasm that involves a segment of the colon.

The roentgenologist often experiences great difficulty in the interpretation of films that show localized spasm, because many such films simulate carcinoma, stricture, and other organic lesions. His efforts to remove the spasm by the administration of drugs such as atropine, benzedrine, etc., are usually futile and disappointing.

Our roentgenologist, Dr. Jacob Leptich, has devised an effective and simple method for differentiating spasm from an organic lesion. When a suspicious filling defect is discovered, the patient expels the enema and a second enema is given which now removes the spasm and results in a smooth film. If persistent after the second enema, the lesion is diagnosed as being of organic nature. The method also has been found to be effective in correcting spasm of the pylorus and duodenum. After the barium meal has left the stomach a second "fill up" reveals a smooth outline instead of the ragged, irregular, spasmodic condition. The irradiated barium meal appears to be an efficient agent in temporarily eradicating gastro-intestinal spasm. The employment of water enemas prior to the examination is bad practice inasmuch as they tend to induce spasm and distortion of the colon. Fecal masses are surrounded by the barium mixture and do not interfere with the diagnostic function of the enema; therefore, the preliminary "cleansing enema" is not only unnecessary but is likely to produce abnormal conditions that cloud the diagnostic picture.

Spasm of the entire colon probably never occurs, at least I have not seen it. *Primary essential uncomplicated spasm* usually involves the descending iliac, and pelvic colon and occurs as a rule in patients of hypersthenic or sthenic habitus, rarely in one of the asthenic habitus. It is usually associated with spasm of the anal sphincter musculature. This condition is described by Hurst as *dyschezia*. The ampulla recti and the cecum are frequently dilated and hypotonic in character. The patient is constipated, and purgatives and enemas cause cramp-like pains in the left abdomen and are ineffective. The feces consist of small, marble-like masses. The iliac colon is palpable as a painful, persistent cord, not the intermittent spasm observed in the normal colon.

The principles of treatment are as follows:

1. Smooth, high calorie, high vitamin diet.

2. Administration of agar-agar or mineral oil, and in severe cases the oil retention enema.

3. Intermittent dilatation of the anal sphincter, and in severe spasm of the recto-sigmoid region, treatment by local applications of magnesium sulphate solution as I have elsewhere detailed.

Psychic spasm occurs in patients suffering from the psychoses. It is usually initiated as an acute attack producing severe abdominal pain and obstinate constipation. Treatment consists in large, frequent, mineral oil retention enemas and the administration of sedative drugs combined with atropine.

Psycho-neurotic spasm is encountered in individuals of unstable nervous system. It occurs in attacks of left-sided abdominal pain accompanied by the expulsion of large strings of mucus. The tough, clear masses sometimes form a cast of the lumen of the gut, this condition usually being termed *mucous colitis*. Ewald and Boas

INTRINSIC SPASM

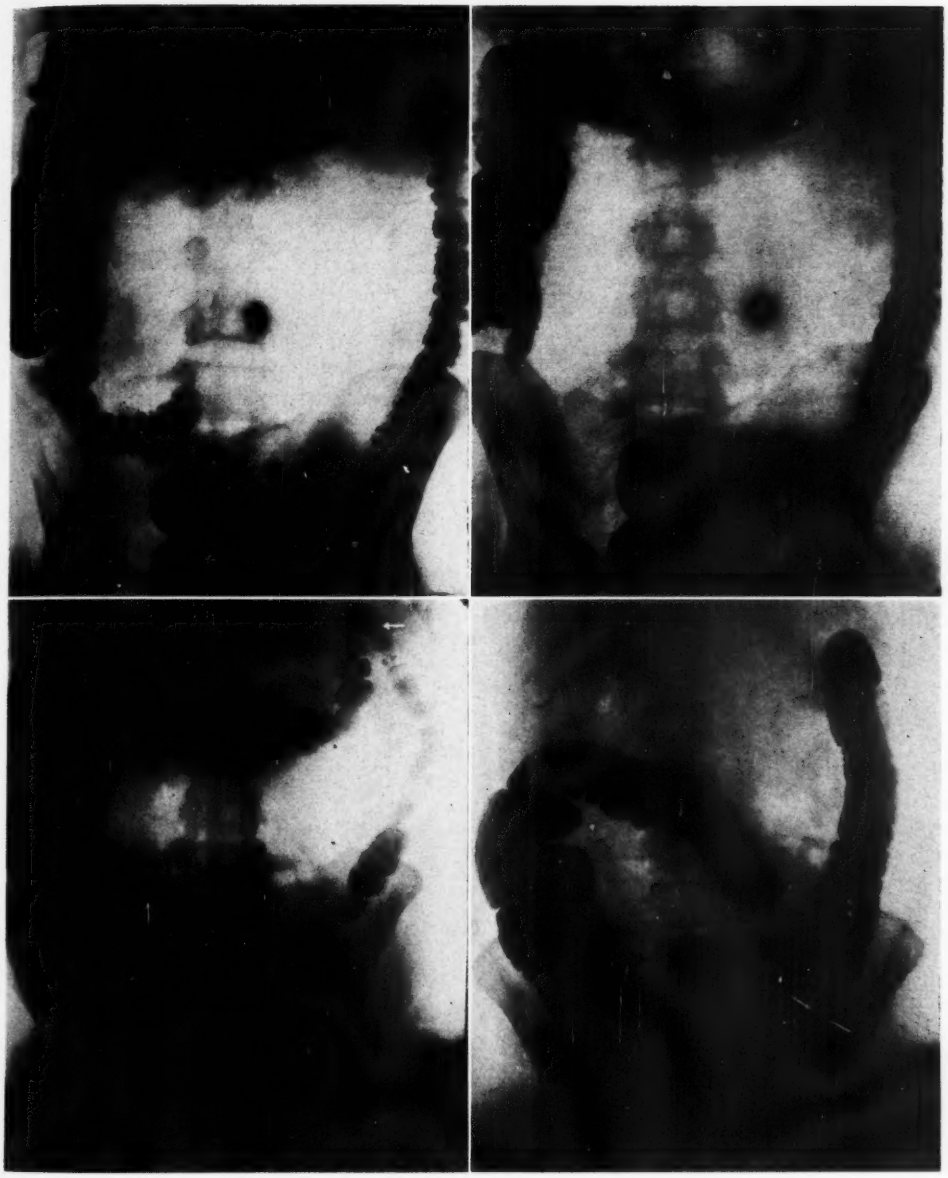

Fig. 1. Case 1 (*upper left*). This film shows a spastic condition of the iliac colon with a number of diverticula (early stage). The patient had used cathartic drugs habitually.

Case 1-*A* (*upper right*). Same patient as shown to the left, Case 1, one month after course of mineral oil retention enemas. The film revealed the smoothing out of the colon and disappearance of the diverticula.

Case 2 (*lower left*). Painful, severe spasm of colon in habitual cathartic-taker, phenolphthalein. Cured by stopping drug and employing a course of oil enemas. One arrow points to a spastic area in the splenic flexure and the lower one to a spasm in the pelvic colon.

Case 3 (*lower right*). Severe spasm in habitual water enema user. Relieved by employing course of oil enemas and a smooth diet

Fig. 2. Case 4 (*upper left*). Painful spasm in cathartic-taker (phenolphthalein). Relieved by stopping drug and giving course of oil enemas. Descending and iliac colon are usual locations for intrinsic spasm.

Case 5 (*upper right*). Case of ulcerative colitis in an abnormal colon. The arrow points to a narrow portion of the colon, raising the question of organic stricture.

Case 5-*A* (*lower left*). The second fill-up enema removed the filling defect, thereby proving that it was not an organic stricture but a localized spasm.

Case 6 (*lower right*). The arrows point to multiple spasms in the iliac colon due to a pathologic appendix. The pain and tenderness was persistent in this region; no pain present in the region of the appendix. Appendectomy resulted in complete disappearance of the symptoms.

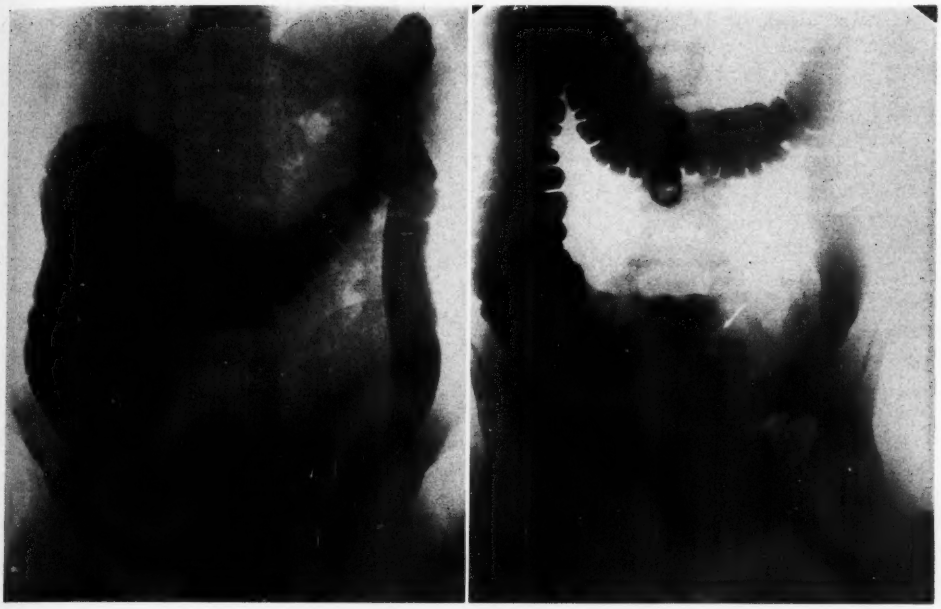

Fig. 3. Case 7 (*left*). The arrows point to the multiple spasms located in the iliac colon. The appendix was retrocecal. Operation revealed that it was bound down by adhesions. No more attacks of colon spasm after appendectomy.

Case 8 (*right*). A pathologic appendix. The arrows point to a spasm which simulates the filling defect produced by carcinoma. A second enema smoothed out the spasm, proving that it was not of organic nature. Cured by appendectomy.

many years ago emphasized that the condition of the colon was not inflammatory in character, that the term *colitis* was a misnomer, and suggested that *colica mucosa* was the correct designation. The syndrome is notoriously difficult to treat, often exhausting our therapeutic resources. The patient deserves a thorough general examination, and all efforts must be made to convince her that she has no organic disease (75 per cent are females). Try to have her understand the true nature of the condition. Of course, avoid all cathartics. The diet should be carefully planned—high in calorie, high in vitamin content, and free from roughage, with small, frequent doses of sedatives combined with atropine. Daily oil retention enema for several weeks' time, followed by agar-agar. Abdominal muscle exercises, regular periods of rest and other general hygienic measures are indicated.

Proctitis, fissure ani, and other rectal lesions may induce spasm of the colon. The therapeutic indications are obvious.

Diseases of the colon, such as carcinoma, benign lesions, polypi, ulcerative colitis, tuberculous, dysenteric, syphilitic, and other ulcerative lesions produce more or less spasm of the colon. A pathologic appendix is a frequent cause. In the establishment of the diagnosis of such lesions, the sigmoidoscope, feces analysis, and the clinical history are essential.

Extrinsic Factors Producing Spasm.—Kidney stones and acute gall-bladder conditions are common causes of colon spasm. Gastric and duodenal ulcer quite often are incriminated as etiologic factors. Many cases of colon spasm occur in psychoneurotic individuals and are erroneously diagnosed as "mucous colitis."

I have a large number of films illustrating spasm induced by many pathologic conditions. In this article I present reproductions of films of patients who have

EXTRINSIC FACTORS

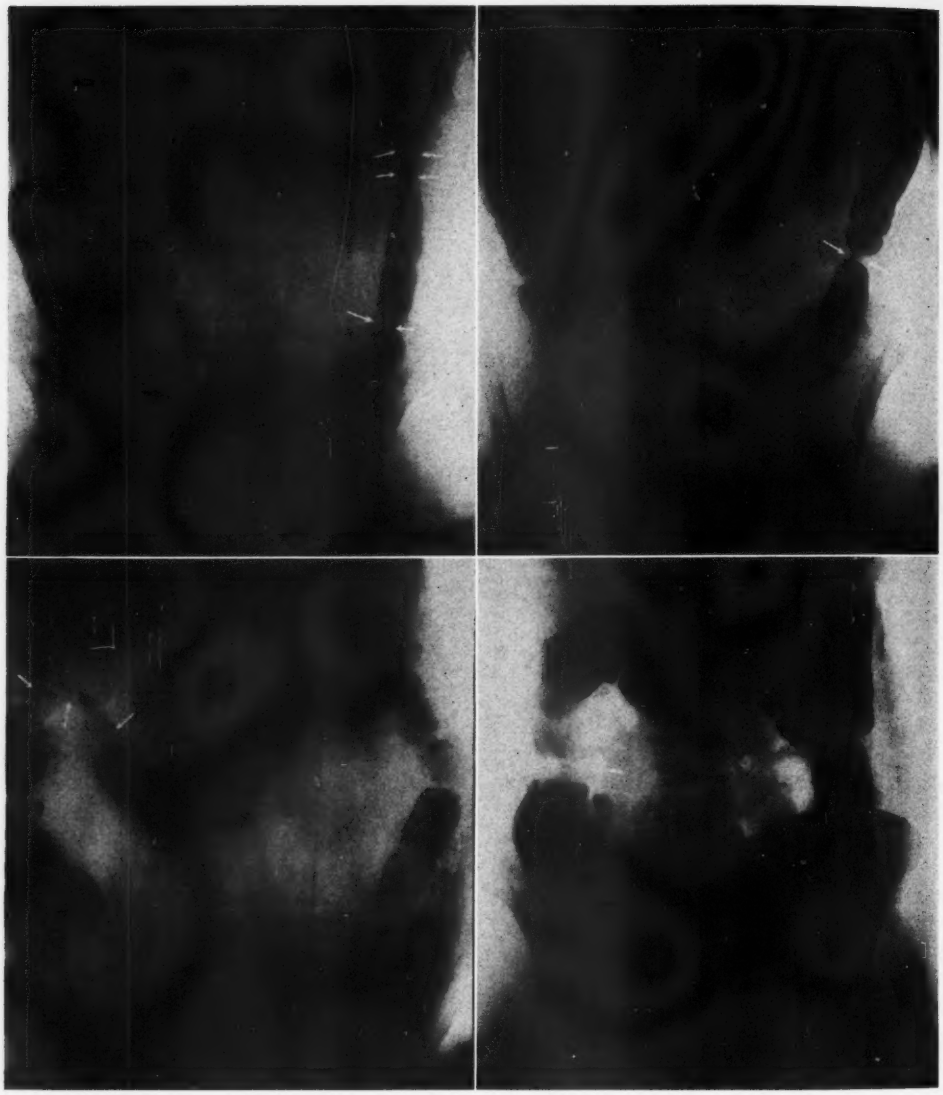

Fig. 4. Case 9 (*upper left*). The arrows point to multiple spasms in the descending colon. The patient had severe pain in this region with expulsion of large masses of mucus. The diagnosis of mucous colitis was made. The urine revealed the presence of red blood cells and a stone was found embedded in the kidney parenchyma. Removal of the stone completely cured the "mucous colitis."

Case 10 (*upper right*). The arrow points to a spasm which one might easily believe to be of organic nature. The kidney serial revealed the presence of a kidney stone that was producing no blocking. Spasm disappeared after operation.

Case 11 (*lower left*). The arrows point to a filling defect at the hepatic flexure. The patient had a fourth degree displacement of the kidney. The operation of kidney fixation revealed that the colon was normal. Following operation a course of oil enemas was given which removed any further colon spasm.

Case 12 (*lower right*). The arrow points to a spasm of the cecum which simulates a filling defect ordinarily seen in carcinoma. Pain was persistent in this region. The patient was operated upon for gallstones and exploration of the colon showed no organic disease.

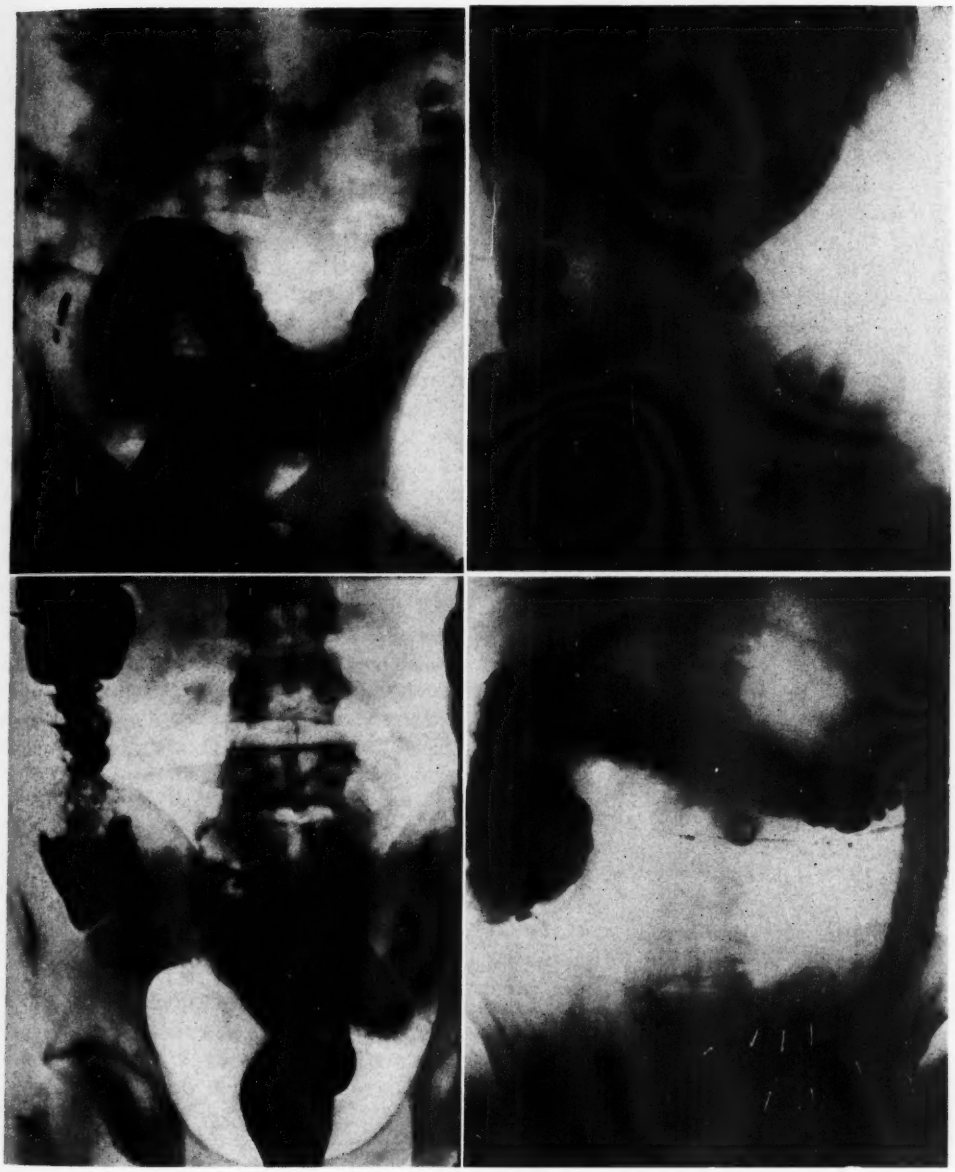

Fig. 5. Case 13 (*upper left*). This film was secured while the patient was suffering from an attack of gallstone colic. Fill-up failed to open up the spasm in this region. At operation the colon was found to be normal. No further spasm afterward.

Case 14 (*upper right*). Severe, painful spasm in case of psychosis. Patient had obstinate constipation but responded well to a course of oil retention enemas.

Case 15 (*lower left*). Severe persistent spasm of cecum in case of psychosis. Tuberculosis or carcinoma was suspected. Spasm disappeared after course of mineral oil retention enemas.

Case 16 (*lower right*). The arrows point to multiple spasm in the iliac and pelvic colon. This region was tender to pressure and was the site of extreme pain. The patient suffered from duodenal ulcer. The spasm subsided under dietetic treatment and a course of oil retention enemas.

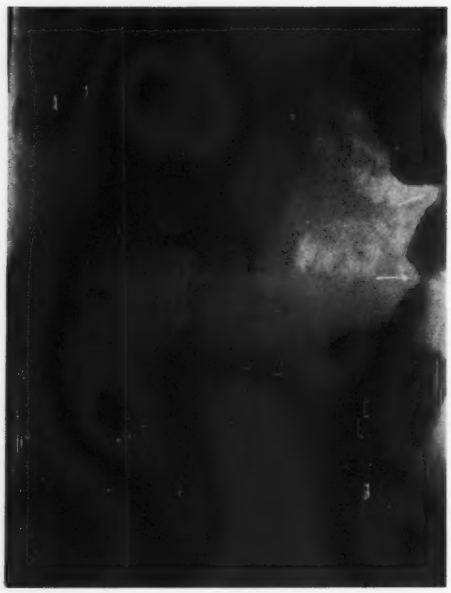

Fig. 6. Case 17. Persistent, painful spasm in case of gastric ulcer. The arrow points to severe spasm of the descending colon which might easily be mistaken for stricture or carcinoma. This area of the colon was extremely sensitive to palpation and localization of severe attacks of pain. Under dietetic treatment and a course of oil enemas the spasm was entirely relieved.

been kept under observation after operation or after the employment of treatment. The follow-up disclosed no recurrence of the former symptoms. For example:

Case 2 had daily attacks of intermittent cramp-like pains of six months' duration.

In Case 5 it was very important to determine whether the defect in the colon was a spasm or an organic stricture.

In Case 6 the attacks of pains were located in the region of the iliac colon and not in the appendix region (four months' duration).

The film of Case 15 was secured before we had known of the second barium enema procedure to abolish spasm. (The appendix had been removed.) The patient complained of severe intermittent pain in the right lower quadrant, and obstinate constipation of two months' duration. He was scheduled for operation when I saw him in consultation. The absence of blood, pus, and tubercle bacilli in the feces caused me to advise postponement and treatment. After the spasm had subsided there was no recurrence of the subjective symptoms.

CLINICAL RESULTS IN SIXTY-NINE PATIENTS TREATED BY A SUBSTERILIZING DOSE OF RADIUM OR X-RAY[1]

By JAMES A. CORSCADEN, M.D., HAIG KASABACH, M.D., *and* MAURICE LENZ, M.D., *New York City*

From the Department of Obstetrics and Gynecology and the Department of Radiology of the College of Physicians and Surgeons, Columbia University

INTRODUCTION

DESPITE the rapid recent advances in our knowledge of the physiology and anatomy of the sexual cycle and despite the availability of pituitary-like and ovarian substances for the treatment of menstrual disorders, there has not been the expected improvement in results following the employment of these substances in the treatment of menstrual disorders. There remain and are likely to remain a number of patients who will require radical therapy by various destructive methods among which radium and x-ray will be of importance. While in about fifteen hundred patients it has been relatively easy to produce a permanent menopause (98 per cent), an attempt to modify or interrupt menstruation without terminating it has been followed by varying results. Those from the standpoint of loss of blood have been generally satisfactory but there has been a wide range of dosage, considerable variation in the duration of amenorrhea following the same doses, and in some an undesired permanent menopause.

Obviously the logical therapy for any disturbed function should aim at the restoration of that function and every device available should be employed to that end. Only if the loss of blood or menstrual distress be great enough to cause definite incapacity should one direct his efforts in the opposite direction and destroy partly or completely one of the three structures essential to menstruation, pituitary, ovarian follicles, or endometrium. We have had little experience with radiation of the pituitary gland or destruction of the endometrium by powerful caustics. It has been necessary in a few cases to remove a normal uterus. Our present study is based on the principle that radium and x-ray destroy ripe Graafian follicles and is directed toward the establishment of an effective yet substerilizing dose.

Radium has been given in the endometrial cavity in doses of from 25 milligrams for 12 hours to 100 milligrams for 24 hours with a filtration of 0.5 mm. silver, 0.5 mm. platinum, or 1.0 mm. platinum with 1.0 mm. rubber secondary filter. The filtration has made some difference in the dosage. To produce a permanent menopause with reasonable certainty, a dose of 1,800 milligram-hours has sufficed with 0.5 mm. platinum. With 1.0 mm. platinum, however, a dose of 1,800 milligram-hours was followed by an increasing number of recurrences of bleeding; 2,000 to 2,400 milligram-hours seems to be necessary. X-ray up to 1923 was given through six abdominal, two lateral, and one posterior portal 3×3 cm. with 100 kv., 25 cm. anode-skin distance, and from 3 to 5 mm. of aluminum filter. This will be designated "old x-ray." After 1923 it was administered through one anterior and one posterior field, 10×15 cm., with 180–200 kv., 50 to 80 cm. anode-skin distance, 0.5 mm. Cu and 1.0 mm. Al filter. Dosages with the "old x-ray" are expressed in total milliampere-minutes. In the average woman of 40, three series of nine exposures of 45 milliampere-minutes each almost always caused amenorrhea. Calculated in roentgens, the total skin dose corresponded to about 800 r, giving an approximate ovarian dose of 250 r. With modern technic the doses are expressed in international roentgens without back-scattering. Depth doses are not given. Variations in the location of the ovaries, where observed, have been

[1] Presented before the Fifth International Congress of Radiology, Sept. 13–17, 1937, in Chicago.

TABLE I.—IMMEDIATE RESULTS
Ages 15 to 25 years. (See note on Table III, p. 208.)

Dose	Continued to Flow			Subsequent Treatment Required			*Bleeding Stopped after (Months)				Permanent Menopause	*Bleeding Returned after (Months)					Character of Return Flow			Subsequent Treatment		
Mgm.-hr. of Radium	Normal	Scant, Irregular	Profuse	X-ray	Radium	Hysterectomy	1	2	3	4		4	8	12	24	60	Normal	Scant, Irregular	Profuse	X-ray	Radium	Hysterectomy
625	2				1					1		1					1					
700			1			1	1							1				1				
"Old x-ray"	2		2	1		1	2		1					3			1	1			1	
Modern x-ray 300 r	1																					
600 r									1					1			1			1		
1400 r							1									1		1				

so great that the depth dose to the ovary seems to be of very small importance in comparison with the other variables. This unreliability may be illustrated by two cases. A woman of 36 with a myoma the size of a three months' pregnancy and an abdomen measuring 18 cm. anteroposteriorly was given 300 r anteriorly and posteriorly. Because of continued bleeding the same dose was again necessary four months later. Only after two years was amenorrhea complete. Another woman, of 26, with a uterus of the same dimensions and an anteroposterior dimension of 25 cm. was given 240 r anteriorly and posteriorly. She stopped menstruating after one period, menstruated again after 13 months, and has been amenorrheic for two years. With identical x-ray factors a relatively large dose of x-ray given to an older, thin woman produced less effect than a small dose in the younger fat patient.

This study includes all of the cases in which an attempt was made to alter, but not terminate, menstruation and some cases in which the induction of a permanent menopause was intended but not accomplished by the initial dosage. It was hoped that from this material it might be possible to establish a "safe substerilizing dose" (Tables I, II, and III).

There were 15 patients between the ages of 15 and 25 (Table I). Brief summaries of the cases are given.

Case 1. G. D., age 22. Para one. One year menorrhagia. Radium, 625 mgm.-hr. Menstruation regular for one year.

Case 2. E. C., age 23. Para one. Two years menorrhagia. Radium, 625 mgm.-hr. Bleeding stopped immediately: returned after four months. Regular for 17 years.

Case 3. R. P., age 25. Para 0. Three years menorrhagia. Radium, 700 mgm.-hr. Bleeding stopped after one month: returned after 13 months, infrequent, scant. Nine years after treatment, abortion at six weeks; again, 15 years after treatment, at eight weeks. Periods scant

and irregular for another two years (17 years).

Case 4. R. S., age 25. Para one. One year menorrhagia. Chronic pelvic inflammatory disease. Radium, 700 mgm.-hr. No reaction. Periods infrequent but prolonged. Pain unrelieved. Hysterectomy for pain two years after original treatment.

Case 5. G. R., age 16. Para 0. Metrorrhagia two years. "Old x-ray," 760 ma.-min. Periods remained irregular, slightly profuse. Radium, 600 mgm.-hr., six months after original x-ray. Periods regular, with occasional skipping, for two years. Bleeding recurred. Dilatation and curettage. Periods regular, somewhat profuse for four years (six years).

Case 6. A. J., age 19. Para 0. Two years menorrhagia, metrorrhagia. "Old x-ray," 850 ma.-min. Bleeding stopped immediately: returned after nine months, regular for three months. No further observation.

Case 7. H. S., age 19. Para 0. Four years metrorrhagia. "Old x-ray," 300 ma.-min. Continued profuse. Three months later, 450 ma.-min. Continued profuse for another four months: 150 ma.-min. Skipped nine months. One profuse period. Dilatation and curettage. Normal for seven years then profuse for one year. Hysterectomy for myoma 12 years after first x-ray.

Case 8. E. K., age 21. Para 0. Purpura hemorrhagica. Two years menorrhagia. "Old x-ray," 500 ma.-min. Bleeding stopped immediately. Two periods in a year, thereafter none. Died two years after treatment.

Case 9. K. M., age 22. Para one. Two years menorrhagia and metrorrhagia. "Old x-ray," 1,200 ma.-min. Bleeding stopped after three months. Returned after 13 months, regular, excessive. Radium, 600 mgm.-hr., 19 months after original x-ray. Permanent amenorrhea for 22 years.

Case 10. R. R., age 24. Para 0. One year metrorrhagia. "Old x-ray," 280 ma.-min. Periods continued every 14 to 16 days, somewhat profuse and painful. Followed three years.

Case 11. L. G., age 25. Para 4. Prolonged menorrhagia. "Old x-ray," 1,050 ma.-min. Periods normal. One year after treatment full term pregnancy: child died at six months. Two years after treatment abortion at two months. Eleven years after treatment spontaneous delivery of normal child.

Case 12. B. K., age 25. Para 0. Fifteen months metrorrhagia. "Old x-ray," 1,435 ma.-min. Periods normal for seven years, then profuse: 200 ma.-min. Periods scant and irregular. Followed 13 years.

Case 13. J. W., age 15. Para 0. Three years menorrhagia, metrorrhagia: 300 r anterior and 300 r posterior. Stopped after three months, returned after 13 months. Became profuse two years after first treatment: 300 r anterior and 300 r posterior. One period. Amenorrhea for two years.

Case 14. J. C., age 21. Para 0. Osteomalacia: 400 r anterior, 200 r posterior; six weeks later 400 r anterior and 400 r posterior. One period five years after treatment.

Case 15. B. C., age 24. Para 0. Four years menorrhagia, metrorrhagia: 150 r anterior and 150 r posterior. Periods normal for one year.

There were 43 women between 25 and 40 years of age. Table II indicates the immediate results of the various dosages in these women and demonstrates the inconstancy of the results. Note that one woman, receiving 600 mgm.-hr. of radium, stopped menstruating after three months and remained permanently amenorrheic (ten years), while 19 who received from 1,200 to 1,800 mgm.-hr. required either hysterectomy or x-ray to control continued or recurrent bleeding. Similarly, of the five women who received 150 r anteriorly and posteriorly by modern technic, one was permanently amenorrheic. One of nine patients receiving a total of 600 r was permanently amenorrheic, as was one patient receiving 700 r.

TABLE II.—IMMEDIATE RESULTS

Ages 26 to 40 years

Dose	Continued to Flow			Subsequent Treatment Required			*Bleeding Stopped after (Months)				Permanent Menopause	*Bleeding Returned after (Months)					Character of Return Flow			Subsequent Treatment		
Mgm.-hr. of Radium	Normal	Scant, Irregular	Profuse	X-ray	Radium	Hysterectomy	1	2	3	4		4	8	12	24	60	Normal	Scant, Irregular	Profuse	X-ray	Radium	Hysterectomy
375			1	1		1																
400							2					2					2					
450							1							1				1				
550									1			1					1			1		
600	2			1		1			2		1	1										
900	1																					
1100		1				1																
1125	1					1																
1200	2		1			1					x											
1400							1				x	1					1			1		
1500									1		x		1						1	1		
1800	2		1	1			2				x	1			1		1		1	1		
2400										1	x	1							1	1		
"Old x-ray"	1		1	1			1		1					1	1		1	1		2		
Modern x-ray 300 r							3	2			1		1	2		1	3	1				
480 r								1						1				1				
600 r	3	1	1	1			3	2			2		1	2			1	2		1		
1200 r							1	1			x		1			1	1		1			1
1500 r							1				x			1			1					

* See note on Table III (p. 208).

Late results in these women showed one who continued to be normal for one year, three for four years, three for six years, and one for twenty-four years. Scant and irregular bleeding persisted in three women for four years, in three for eight years, and in one for twelve years. Hysterectomy was performed on six patients, two for continued bleeding from a normal uterus, one for continued bleeding with a large fibroid, two because patients with small fibroids preferred hysterectomy to a permanent menopause, and one because of a misinterpretation of the nature of scant bleeding (fear of carcinoma which did not exist). Thirteen women were retreated by x-ray or radium; all became amenorrheic and so remained for two years, six years (three cases), and eight years (three cases), leaving four whose treatment has been too recent for purposes of a late observation.

The 11 patients in Table III over 40 years of age are selected merely to bring out the fact again that small doses of radiation terminated menstruation in some, whereas larger doses failed in others. With efficient methods for controlling distressing menopause symptoms in the occasional case, we can see little reason for a partial dose in women of this age.

The conclusion from these observations is that the substerilizing dose cannot be satisfactorily expressed numerically. If menstruation must be preserved, small initial doses (150 r, 25 per cent E.S.D. to one anterior and one posterior field) must be given. Radium is seldom employed for the reasons given later.

DYSMENORRHEA

Dysmenorrhea was a major symptom in nine patients. In two cases the menstrual distress was an exacerbation of a chronic inflammatory symptom and was slightly relieved by a temporary menopause. One patient, aged 31, was operated upon for endometriosis and retained one ovary. The recurrent dysmenorrhea was treated by x-ray. For six years menstruation has been infrequent and usually somewhat painful. Amenorrhea between the periods has been accompanied by hot flashes. We believe that a permanent menopause would be more satisfactory. However, this assurance that endometriosis can be terminated by sterilization permits us to leave untouched the uninvolved ovary in these cases in the hope that future child-bearing may be possible.

The fourth case of dysmenorrhea followed excision of an ovarian cyst in a woman of 26. Terrific attacks of pain and vomiting preceded each irregular triweekly period. Exploratory laparotomy, abandoned because of adhesions, left her with a fecal fistula which healed spontaneously. After radiation, menstruation and the attacks ceased. Eight months later a typical attack of pain was followed by a period. Permanent amenorrhea was established by further x-ray and radium. Since then there has been perfect health marred only by occasional hot flashes which required no treatment (eight years). The fifth case of dysmenorrhea persisted in a woman despite resection of large polycystic ovaries. During the temporary menopause the pain ceased but returned with menstruation and was terminated by further radiotherapy. Incidentally the enlarged ovaries became atrophic. The sixth patient, aged 27, was obese. The pelvic examination was normal. Vomiting and pain were so disabling as to endanger her position as an executive. Following radiation she was amenorrheic for eight months and free from pain. Her obesity disappeared. With the return of menstruation the distress also returned and she again became obese. She refused a permanent menopause and has been greatly relieved by psychoanalysis. The other three patients ($33\frac{1}{3}$ per cent), with apparently normal pelvic organs, remained completely free of pain after the return of their periods.

FIBROMYOMA

Among the women between the ages of 25 and 40 there were six cases of fibro-

TABLE III.—IMMEDIATE RESULTS

Ages over 40 years

Dose	Continued to Flow			Subsequent Treatment Required				*Bleeding Stopped after (Months)				Permanent Menopause	*Bleeding Returned after (Months)					Character of Return Flow			Subsequent Treatment		
Mgm.-hr. of Radium	Normal	Scant, Irregular	Profuse	X-ray	Radium	Hyster-ectomy		1	2	3	4		4	8	12	24	60	Normal	Scant, Irregular	Profuse	X-ray	Radium	Hyster-ectomy
500											1	1											
600								3		1		2	1		1				2			1	
1200			1		1					1					1				1				
1800			1		1			1							1			1					
"Old x-ray"																							
Modern x-ray 300 r			1		1																		
400 r											1				1			1					
600 r																							

* The term "bleeding" includes all types with regular menstruation or irregular bleeding. The columns to the left indicate those cases which continued to bleed after the treatment. Those to the right indicate the cases in which the bleeding stopped, either temporarily or permanently.

myoma smaller than the size of a two-months' pregnancy. One woman, receiving 600 mgm.-hr. of radium, became permanently amenorrheic (10 years). One, after 1,125 mgm.-hr., had an hysterectomy for continued bleeding. Two, after 900 mgm.-hr., required supplementary x-ray and became permanently amenorrheic. Following x-ray, one woman chose hysterectomy rather than a permanent menopause when her periods returned. The periods of one woman became scant and irregular; the size of the uterus remained unchanged. Eight women had myomas the size of a three- to four-months' pregnancy. One, following 1,200 mgm.-hr. of radium, required an hysterectomy for continued bleeding. One, after 1,200 mgm.-hr., had regular periods, became pregnant after 18 months, aborted, and was not followed. Two, receiving 1,800 mgm.-hr., required supplementary x-ray for continued bleeding and became permanently amenorrheic. One, treated by "old x-ray," continued to have scant, infrequent periods for 10 years. One, treated by modern x-ray (600 r), required supplementary x-ray for continued bleeding and was scant and irregular for two years, then amenorrheic for 10 years. One, receiving 480 r, stopped after two months, had one period after 13 months, and has been amenorrheic for two years. In all of these women the uterus has shrunk to normal dimensions. One woman, aged 33, had a uterus that ex-

tended to the umbilicus. Hysterectomy was abandoned because of adhesions. She received 600 r and was amenorrheic for eight months. The mass shrank to the size of a three-months' pregnancy and then began to grow, reaching its original size in two years, when the periods returned. Following additional x-ray, she again became amenorrheic. The mass is somewhat smaller in size (six months later).

To summarize: the substerilizing dose for myomas has not been satisfactory. In only two patients did the periods continue and the mass shrink. The others either became amenorrheic after a small dose, required supplementary radiotherapy to control bleeding and the size of the mass, or were operated upon.

PREGNANCY

Six women have become pregnant. Four have been reported in part (Murphy, 1929) but are included for the sake of completeness. One woman, aged 36, with a fibromyoma the size of a three-months' pregnancy, received 1,200 mgm.-hr. of radium. The periods were regular for 18 months. She became pregnant, had a miscarriage at four months, followed by slight puerperal fever. The fetus was grossly normal. No follow-up. A patient, aged 25, was given 700 mgm.-hr. of radium for primary metrorrhagia. The periods became infrequent and somewhat scant. A pregnancy, nine years after treatment, aborted at six weeks, and another, occurring 15 years after treatment, aborted at eight weeks. She was curetted each time without complications. A patient, aged 28, received 600 mgm.-hr. of radium after which the periods became normal. She became pregnant four years after treatment, and aborted. Her second pregnancy, one year later, was normal and the child was normal. A patient, aged 25, received a total of 1,050 ma.-min. of the "old x-ray," after which her periods became normal. The first pregnancy, one year after treatment, was normal. The child was normal but died at the age of six months, of unknown cause. The second pregnancy, two years after treatment, was aborted spontaneously at two months. The third pregnancy, eleven years after treatment, resulted in the normal delivery of a normal child who has showed abnormal behavior, requiring institutional care at the age of nine. There is ample cause in the heredity and environment, however, adequately to account for this. A patient, aged 28, received 532 ma.-min. of "old x-ray," after which her periods became normal. Pregnancies, four and ten years after treatment produced normal children, now 16 and 12 years old, respectively, in perfect health and in advanced grades in school. A patient, aged 30, given 500 mgm.-hr. of radium for primary menorrhagia, became pregnant ten years after treatment. By Cæsarean section a slightly premature, otherwise normal, child was born, but died, aged six weeks, of epidemic enteritis.

A summary of these few cases showed that of 11 pregnancies only four children have lived beyond infancy, five having aborted and two dying at six weeks and six months, respectively. If these proportions existed in a series large enough to make the figures valid, it would appear that radiotherapy exerted a harmful influence on subsequent pregnancies. Fortunately the larger collections of cases do not seem to bear this out (Murphy, 1929; Miller, 1936; Kraemer, 1930).

CHOICE OF PROCEDURE

The management of a young woman suffering from a menstrual disorder without gross pelvic lesions is conducted about as follows:

After a complete diagnostic study, attempts are made to establish a normal physical and mental hygiene; anterior pituitary-like substances and or Progesterone will be given, occasionally rationally, more often empirically. At some point in the procedure, not always at the beginning, a curettage will usually be performed. Often this will control the bleeding for several months. If it does so for from six to eight months, it is frequently wise to re-

peat the curettage several times rather than institute any of the destructive measures now under discussion. There comes a time, however, when all devices have failed. The anemia is severe; transfusions may be necessary. The choice narrows down to three procedures: (1) x-ray treatment of the pituitary gland; (2) destruction of the endometrium by caustics or excision; (3) destruction of the ripe Graafian follicles by x-ray or radium. With the first type of therapy we have had little experience nor have we applied powerful caustics to the endometrium. It has been necessary to choose between some form of hysterectomy and radiation of the ovaries. In our hands this choice hinges upon the desirability of future childbearing. If a woman has two or more children, it is often simpler for all concerned to perform an hysterectomy and leave the ovaries *in situ*. Contrary to some recent observations (Kretzschmar, 1935), it is our experience that menopause symptoms do not soon follow this procedure. The general appearance and sensations of the patients remain unchanged. Several women, followed more than 20 years, have never been conscious of hot flashes.

If, on the other hand, the woman desires to have children, an attempt at a partial sterilizing dose is the more conservative procedure. While there is always some risk of injuring the germ plasm and thereby predisposing to some anomaly in the child, the evidence collected by Murphy (1929) and Miller (1936) has not indicated that this has happened. Among our cases the two happy families with healthy children growing toward maturity compensate for the several failures. If, unfortunately, a permanent menopause should be established, the endocrine deficiency can easily be made up. The psychological aspects, however, are controlled with greater difficulty. If the therapist has studied the manifestations of the menopause, he will, before administering radiotherapy, have prepared the patient's mind for a permanent menopause. The management of a woman suffering from symptoms of an unanticipated menopause can be a difficult problem indeed.

The management of fibromyoma in a young woman is highly individual. In a case in which treatment is necessary, some form of excision is nearly always advised and radiation given only when an operation is contra-indicated. In general, a partial dose has not been satisfactory. Bleeding is likely to continue and with the resumption of menstruation, the mass may increase in size. It is wiser in most instances to terminate menstruation and to treat the menopause, if hot flashes are severe, by the administration of estrogenic substances.

Dysmenorrhea, absent during the period of amenorrhea, usually recurs when menstruation returns. After all other efforts (general hygienic, endocrine, and psychic) have failed and a justifiable dilatation and curettage with insertion of a stem pessary has been attempted, frequently some radical therapy must be given. The choice then rests between a sympathectomy and radiotherapy. In this clinic results of sympathectomy have been good enough to make it preferable to a temporary menopause, despite the dangers incident to the laparotomy. If radiotherapy is instituted, it should be given with a clear understanding that the menstrual distress is likely to recur with the return of the periods.

DISCUSSION

Attempts to modify, but not terminate, menstruation were made almost as early as the discovery of the effect of the rays upon the follicular apparatus of the ovary (Gauss, 1911). Technics have been determined by two lines of thought: First, that there was a direct effect upon the endometrium, blood vessels, or myometrium which in some way modified the menstrual flow; second, that the lasting effects of this method were brought about by the destruction of Graafian follicles. The evidence which we have would point toward the latter mechanism. Specimens of uteri which received a sterilizing dose of radium showed only a small proportion of

the endometrium to be affected by the radium (Corscaden, 1935). Secondly, the absence of menstruation, either temporary or permanent, was almost always accompanied by hot flashes. Thirdly, examinations of the blood and urine of women made amenorrheic by radium or x-ray have shown the characteristics found in the spontaneous menopause—absence of estrone and increase of prolan. We accept the principle, then, that while radium, by its local action, may destroy part of the endometrium and may, for a cycle or two, modify menstruation thereby, the essential action of radium and x-ray is upon Graafian follicles in any prolonged modification of the sexual cycle.

Of the two agents radium or x-ray, we most often employ the latter. If pregnancy occurs later on in life, the uninjured uterine cavity will be more likely to retain the ovum. Secondly, control of dosage is more difficult with radium, because the intensity of the irradiation is reduced in inverse proportion as the square of the distance from the radium. The difference of a centimeter or two in the distance between the radium in the uterus and an ovary may make a difference of as much as 50 per cent in the amount of radiation reaching the follicles. On the other hand, in a case in which a patient is suffering from an extremely profuse hemorrhage, the good effects of a dilatation and curettage and insertion of radium are almost always immediate because of the local caustic effect of the radium. Only in these cases is radium preferred.

In the literature there is a fair unanimity of opinion that in a young woman a dose of from 23 to 29 per cent E.S.D. will be followed by a definite and temporary amenorrhea (C. J. Gauss, 1930); (Kadisch, 1921, 1925). Schneider (1930), varying the dose according to age, constitution, and indication, can produce an amenorrhea of predictable duration. Our experience does not confirm this. The inconstancy of the radium results may be explained on mechanical grounds. Any ovarian tissue lying at a distance from the uterus would receive an ineffectual dose of radiation. Variations in the results from x-ray are more difficult to explain (*cf.* C. J. Gauss and Wintz, 1930). If a reasonable guarantee must be given that menstruation will return, an initial dose of 150 r anteriorly and 150 r posteriorly, given in two sittings, is safe. If the woman is nearing 40, an even smaller initial dose may be needed. If, because of the severity of the symptoms, a more certain effect is desired and the risk of a permanent amenorrhea not so objectionable, one would be justified in giving an initial dose of 300 r anteriorly and 300 r posteriorly in four treatments. Except for acute bleeding, radium should not be employed.

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HEREDITARY EFFECTS OF X-RAY RADIATION[1]

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From the Carnegie Institution of Washington

I SHALL introduce this discussion of the hereditary effects of x-ray radiation by outlining the general biological principles involved.

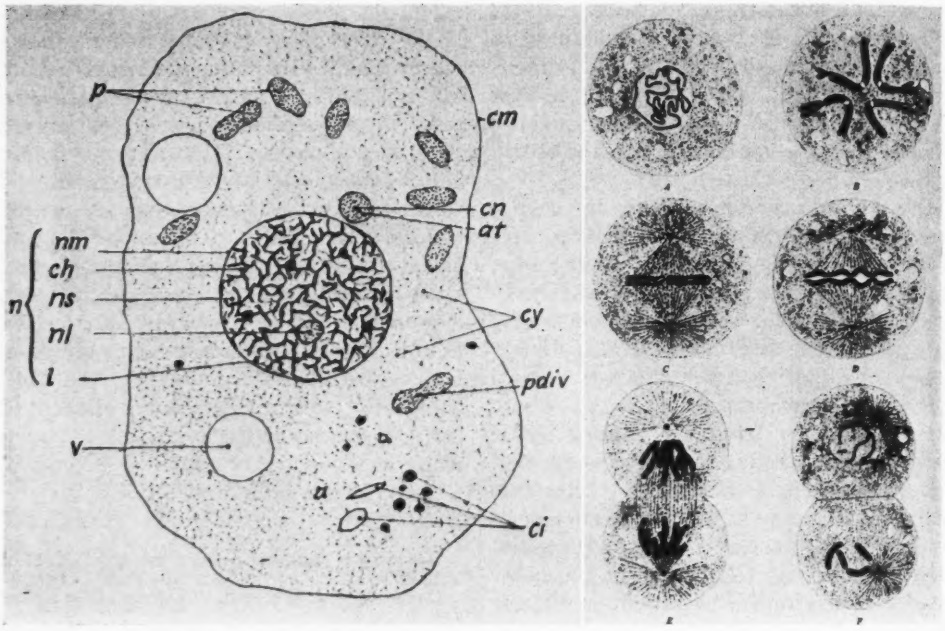

Fig. 1 (*left*). Diagram of a typical cell: *cm*, cell membrane; *cy*, cytosome; *n*, nucleus; *nm*, nuclear membrane; *v*, vacuole. (After A. F. Shull.)

Fig. 2 (*right*). Semi-diagrammatic representation of somatic cell division of *Ascaris*, a parasitic thread worm. *A*, early stage, chromatin thread slightly condensed; *B*, chromatin thread has formed into chromosomes which are arranged across the middle of the spindle; *C*, same as *B*, viewed from another angle; *D* and *E*, chromosome halves moving apart, cell body beginning to divide; *F*, division of cell body complete. (After A. F. Shull.)

PHYSICAL BASIS OF HEREDITY

The majority of living organisms, both animals and plants, are composed of a large number of cells. Through complicated processes these cells differentiate in various regions of a developing organism, thus building up different organs of a body. Generally, a living cell is composed of two parts: cytosome and nucleus. In each of these parts a number of definite constituents can be distinguished (Fig. 1). Since certain nuclear constituents play the major rôle in heredity, I shall focus attention on the nucleus and disregard the other parts of a cell.

Most living organisms begin life as a single cell which follows a union of a female gamete, or ovum, and a male gamete, or sperm. From this first cell the new individual acquires its volume through cell division and its form through cell differentiation. As the first step in cell division the diffuse mass of the nucleus becomes visibly organized into its constituents. Long delicate threads, known as chromosomes, be-

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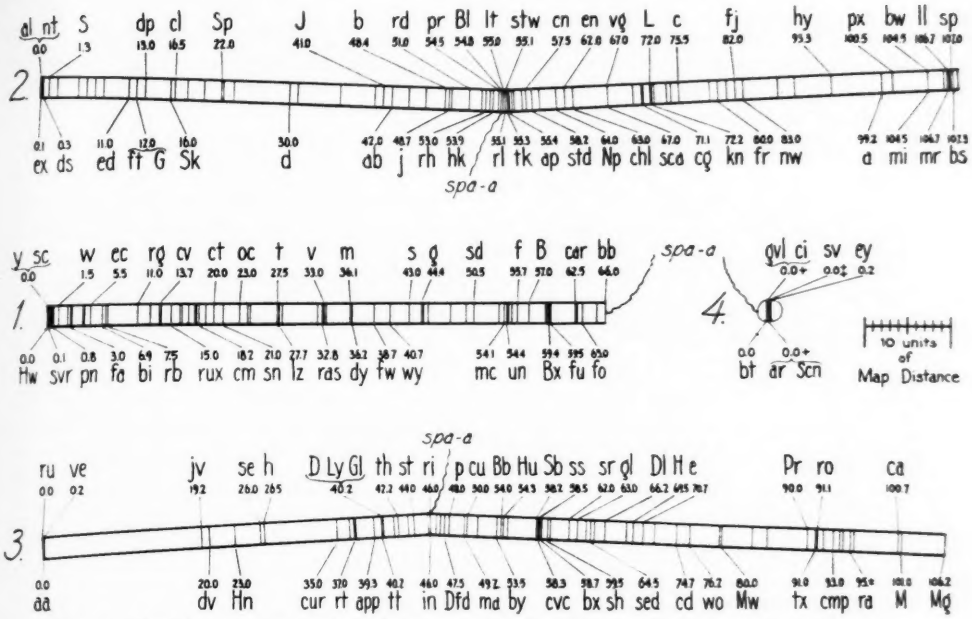
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Fig. 3. Genetic maps for the four chromosomes of *Drosophila melanogaster* (C. B. Bridges).

come clearly defined (Fig. 2-*A*). In most organisms they condense to form sausage-shaped bodies (Fig. 2-*B*). These chromosomes then become arranged in the center of the cell (Fig. 2-*C*), where each is seen distinctly to be split longitudinally (Fig. 2-*D*). Subsequently one half of each chromosome moves to one pole, the other half, to the opposite pole of the cell (Fig. 2-*E*). Around each of the two groups of chromosomes a new nucleus is organized; the formation of a cell wall traversing the cytoplasm between the two nuclei completes the division (Fig. 2-*F*).

To the geneticist chromosomes are the most important constituents of a cell because they are carriers of hereditary units known as genes. Genes possess a unique capacity of self-reproduction which is one of the most important characteristics of living matter. All evidence indicates that they reproduce exactly, and moreover, that if any change occurs, the gene reproduces in its changed form. Experimental evidence suggests that genes possess a high degree of stability. It is known that changes in genes do occur spontaneously, but, as a rule, the frequency of such changes is very low. It is known, also, that genes are very resistant to the influence of ordinary environmental fluctuations. So far the only agents known to induce gene changes with certainty are x-rays and related radiation. High temperature also induces such changes, but, the effective range being high, is too injurious to the organism to be of extensive practical use.

Since genes are ultramicroscopic, our knowledge about them must be obtained through indirect methods. It is estimated that every cell of the "vinegar fly" (*Drosophila melanogaster*) has about 5,000 different genes. Some of them, a small proportion, can be recognized by the effect they produce on the organism and thus can be studied by breeding methods. These studies show that every gene has a fixed location in a chromosome. The location of the genes which produce these visible effects can be determined, and thus the so-called "genetic maps" can be constructed. Figure 3 shows such maps for *Drosophila melanogaster*.

Current genetic concept assumes that the whole complex of genes of a living cell forms a balanced biological system. The appearance of the whole organism, the activity of a group of cells and even of a single

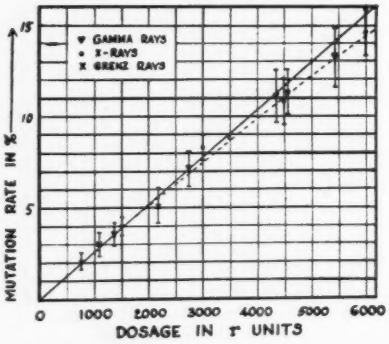


Fig. 4. Action of different wave length on the rate of mutations in *Drosophila melanogaster*. Grenz rays = 10 kv.; x-rays = 50–150 kv.; gamma rays = from radium. (From Timofeeff-Ressovsky and Zimmer, 1935.)

cell is determined by the make-up of that system. Changes in genes affect the balance of the whole gene system. For example, if a change occurs in the white locus of *Drosophila*, that change, if present in a fertilized egg, will affect the gene system in such a way that the individual will develop white eyes instead of developing the normal red eyes. Similarly, a change in other genes again shifts the balance of the system and the observed result is the appearance of short wings, or cut wings, or small eyes, or some other definite hereditary character. Thus, genes are called "bearers of hereditary characteristics" or "units of heredity." They produce visible effects through their functioning in individual cells. Moreover, experimental evidence indicates they play an important rôle in the vital processes. Cases are known in which the elimination of even a single gene out of a set of 5,000 supposedly present in *Drosophila* upsets the normal activity of the cell to such an extent that its normal reproductive capacity is lost. It is known that every cell contains a large number of these ultramicroscopic particles, the genes, and that these genes have a high degree of individuality and perform important functions which, in many cases, are vital to the cell.

HEREDITARY EFFECTS OF X-RAYS: DIRECT OBSERVATIONS

Since chromosomes are carriers of genes and genes are determiners of hereditary characteristics, any detectable change in chromosomes should affect the hereditary capacity of a cell. Therefore, direct observations of chromosomes immediately following an x-ray treatment should reveal the nature of any induced changes.

One of the great difficulties in making direct cytological observations of x-ray effects is the fact that chromosomes are visibly differentiated in dividing cells only and that it is technically difficult to obtain large enough numbers of dividing cells to make the observations. For this purpose, plants seem to be more suitable material than animals. Huskins and Hunter's (1935) observations on *Trillium* indicate that x-ray treatment prevents or retards cell division and induces cell degeneration. The same authors and several others (Stone, 1933; Mather and Stone, 1933; Mather, 1934; Nebel, 1936) observed that cells dividing immediately after the treatment had sections of different chromosomes interchanged and pieces broken off. Such chromosomal aberrations are likely to affect the normal functions of a cell in which they are present. Interchange of sections is frequently accompanied by either a change or a loss of a small section of the chromosome at the breakage points. Such changes or losses produce heritable abnormalities which frequently are lethal, *viz.*, they kill the organism. If as a result of treatment a chromosome becomes broken, an unattached piece may be lost during cell division, such a loss producing a deficiency for the genes located in the lost section and possibly having a lethal effect on the organism.

Cytological observations made immediately after treatment indicate, therefore, that x-rays induce pronounced changes in the hereditary material of a treated cell.

GENETIC RESULTS

For an analysis of hereditary changes, breeding methods are more sensitive than cytological methods. By breeding methods, however, only those changes can be detected which show up in the offspring. This limits the applicability of the method to the group of hereditary changes which are not too large to be injurious, nor too small to be undetectable. In analyzing the results of numerous experiments in which x-rays were used, it is well to keep in mind that only an unknown fraction of the changes actually induced has been registered in these results.

Drosophila melanogaster is the best known organism as far as heredity is concerned because the breeding of this species offers certain unique advantages. It is not surprising, therefore, that a great deal of our knowledge concerning the hereditary effects of x-rays has been derived from studies made on these flies. In this report the results obtained in work with *Drosophila* will be used to a large extent.

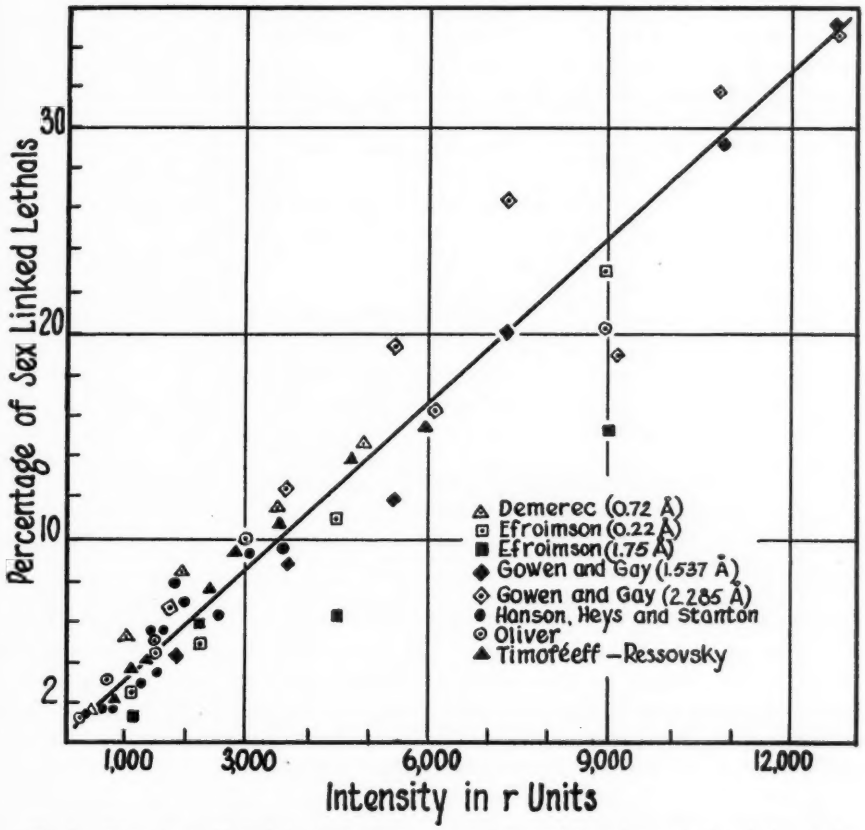


Fig. 5. Percentage of lethals in the X-chromosome of *Drosophila melanogaster* in relation to the intensity of radiation. (From Schultz, 1936.)

It has been found that x-rays can influence hereditary traits by producing breakages in chromosomes and also by inducing changes in genes. Evidence is available which indicates that, very frequently, at the point of a chromosome break, a change in a gene also occurs. Since, in a large proportion of cases, these changes represent either an inactivation or

an elimination of genes, it can be assumed that destructive processes are going on in places where changes are occurring. The cases, the x-ray treatment produces changes in the genes rather than gene eliminations.

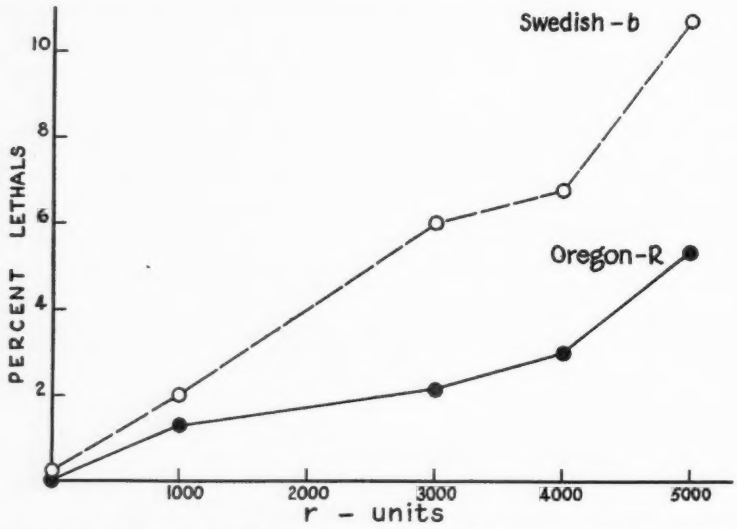


Fig. 6. Percentage of X-chromosome lethals induced by identical treatment in two strains of *Drosophila melanogaster*.

experimental evidence indicates also that a large proportion of detectable hereditary changes are lethal changes. The experimental evidence indicates, too, that these effects may be caused by a loss or inactivation of genes more commonly known as "gene deficiencies." It is not known how this process takes place. However, in order to eliminate a gene it is not necessary to destroy it; it is sufficient to induce a change which would deprive the gene of its power to reproduce. After one cell division such a gene is automatically eliminated from the gene complex of the daughter cells. It seems quite probable that many eliminations of genes result from such processes.

It is known, however, that not all changes induced by x-ray radiation are the result of loss of hereditary-bearing material. In several cases changes were induced in normal genes and then, by further treatment, the transformed gene was changed back into the original form. This evidence offers positive proof that, at least in some

Numerous experiments with *Drosophila* indicate that the effect of x-rays is independent of the wave length within a range of about 0.01Å. to 2.2Å. (Schechtmann, 1930; Ephroimson, 1931; Hanson, Heys, and Stanton, 1931; Timofeeff-Ressovsky and Zimmer, 1935; Fricke and Demerec, 1937). Figure 4 presents graphically the data of Timofeeff-Ressovsky and Zimmer (1935) showing that similar dosages produce similar effects irrespective of the wave length used.

It has been shown, also, that the frequency of lethals induced by x-ray treatment is directly proportional to the dosage applied. Data dealing with this problem were summarized by Schultz (1936) and presented graphically in the chart shown in Figure 5. It should be noted, however, that Schultz used a correction factor for certain data, bringing all curves to the same level.

Experiments by Patterson (1931) and by Timofeeff-Ressovsky (1934) show that applying a certain dosage in fractions did not have any influence on the induced mu-

tation rate. Apparently there is no evidence of recovery in the case of hereditary effects. As long as the same cells are treated, the effect is similar irrespective of whether the increase in dosage is accomplished through a longer continuous or fractioned treatment.

Another important contribution to the problem of x-ray action came from experiments by Muller (1928) and by Harris (1929), who showed that the frequency of lethal mutations was similar in the sperm used immediately after irradiation and in the sperm tested several days after the treatment.

All these facts, namely, the independence of the frequency of changes from wave length, the direct proportionality between dosage and the frequency of changes, absence of delayed effect, and results with fractional treatment suggest that changes in genes are produced directly by electron hits. This hypothesis has been elaborated in detail by Timofeeff-Ressovsky, Zimmer, and Delbruck (1935).

However, the results of recent experiments brought out new facts which are not in agreement with the direct hit hypothesis. Dubovskij (1935) reported that several *Drosophila* lines differed significantly in the frequency of lethals induced by a similar treatment. I have observed that the Oregon-R stock of *Drosophila melanogaster* has a significantly lower rate of induced mutations than all other wild-type stocks tested so far. In Table I and Figure 6 results of experiments are shown in which Swedish-b and Oregon-R stocks were given a simultaneous treatment with certain x-ray dosages. It is evident from these results that in every instance the Oregon-R stock had a lower rate of mutation than the Swedish-b stock. Since in these experiments all external factors were identical for every dosage used, the differences observed can be attributed only to the differences in biological factors. To explain these results by the direct hit hypothesis it is necessary to make several assumptions which are not needed if it is assumed that the action of x-rays on the heredity-bearing material is indirect. The changes in genes and chromosomes are probably of the nature of sensitized reactions induced by the transfer of energy from neighboring activated molecules (Fricke and Demerec, 1937).

In the majority of x-ray experiments with *Drosophila*, treatment was given to males since they are more convenient to use for this purpose than females. An adult male has a supply of mature sperm which, under normal conditions, lasts for several days. In treating males, therefore, changes induced in mature sperm are produced.

Sterility is the most noticeable aftereffect observed in males treated with heavy dosages. Although no exact figures are available, there is strong probability that a certain proportion of that sterility is due either to the killing or the inactivation of the sperm within the treated male. Data

TABLE I.—EFFECT OF IDENTICAL X-RAY DOSAGES ON THE FREQUENCY OF X-CHROMOSOME LETHALS IN TWO STRAINS OF *Drosophila melanogaster*

Dosage r-units	Oregon-R			Swedish-b		
	Chromosomes Tested	Lethals	Percentage of Lethals	Chromosomes Tested	Lethals	Percentage of Lethals
Control	3,049	2	0.066 ± 0.03	1,627	3	0.18 ± 0.07
1,000	1,000	13	1.30 ± 0.24	1,015	20	1.97 ± 0.30
3,000	465	10	2.15 ± 0.45	383	23	6.01 ± 0.82
4,000	617	19	3.08 ± 0.47	458	31	6.77 ± 0.79
5,000	405	22	5.43 ± 0.76	233	25	10.73 ± 1.37

obtained by Timofeeff-Ressovsky (1931) indicate that a high death rate during embryonic development is responsible for other cases of sterility (Table II). It is evident from these data that the sperm was so affected by irradiation as to cause a high death rate among the offspring.

Ample experimental evidence is available to show that from fertilizations with such treated sperm a large proportion of the viable offspring carries heritable changes which, in the majority of cases, are abnormalities of various types. Some of these are dominant and show up in the first generation offspring; others are recessive and may remain unobserved for generations until a chance fertilization brings together a male and a female gamete carrying the identical abnormality.

Abnormal individuals frequently appear among the first generation offspring of the treated sperm. Some of them are mosaics with one part of the body different from the rest. An example of such mosaicism is described by Astaurow (1937) in the silkworm (*Bombyx mori*). Females of a race with light colored caterpillars were crossed with irradiated males of a race with dark colored caterpillars. The first generation caterpillars are expected to be dark colored but a number of them were mosaics with one part of the body dark and the other light colored (Fig. 7).

All these effects of irradiation can be traced to changes in the heredity-bearing material, chromosomes and genes, and such changes are readily induced. It has been estimated (Demerec, 1936) that a dosage of 2,500 r-units produces in irradiated *Drosophila* males, on the average, approximately one change per sperm.

Irradiation produces similar changes in ova and in somatic cells. It has been shown by Patterson (1929) that by irradiating *Drosophila* embryos or larvæ, distinct patches may be induced on the body of the adult fly—these patches having similar characteristics to those induced by the treatment of the gametes. The size of the patches corresponds to the stage of development at which the treatment is applied—large patches indicating changes which took place early in development, and small patches, those which occurred late. This evidence is a conclusive proof that x-ray irradiation induces changes in the hereditary material in somatic cells.

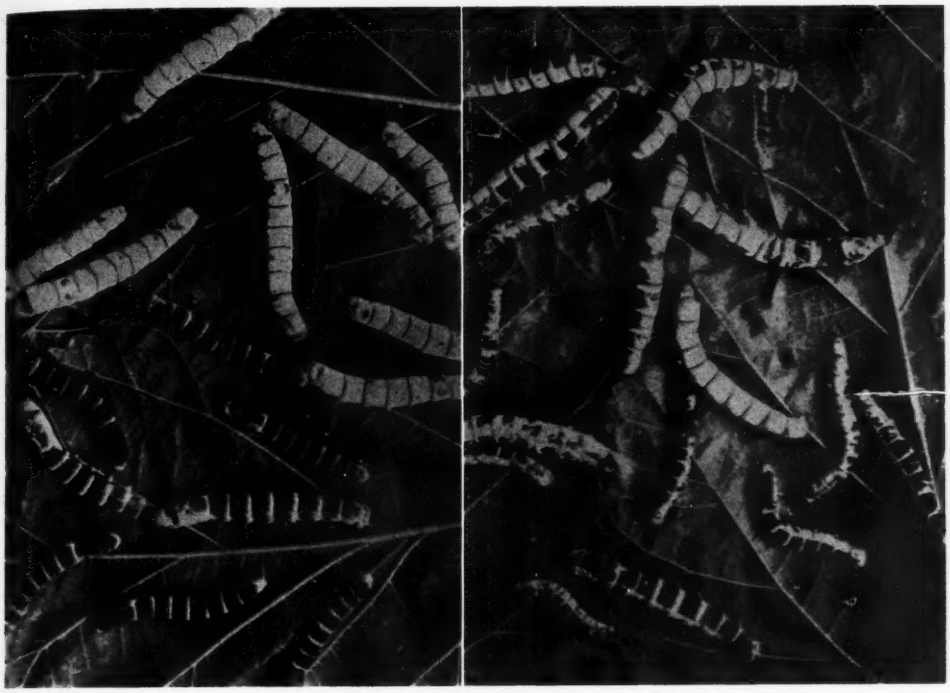
CONCLUSIONS

X-rays have been used extensively in genetic research since Muller's discovery (1927) of their influence on heredity and the high frequency with which they are able to induce hereditary changes. X-rays and related radiations are the most powerful agencies known at present for inducing hereditary changes, and they have made an extremely important contribution to theoretical genetics.

One important fact which should be kept in mind when the effect of x-rays is considered is that a great majority of detectable hereditary changes, both spontaneous and induced, are detrimental to the organism. A great many of them are lethal to organisms as a whole and some are even lethal to a single or to a few cells.

TABLE II.—MORTALITY OF EGGS AND LARVÆ IN THE PROGENY OF *Drosophila melanogaster* MALES IRRADIATED WITH ABOUT 2,500 R-UNITS (AFTER TIMOFEEFF-RESSOVSKY, 1931)

Males	Number of		Percentage of Eggs Mortality	Number of Flies Emerged	Percentage of	
	Eggs Laid	Larvæ Hatched			Larval and Pupal Mortality	Eggs Developing into Adults
Treated	1,829	437	76.1	235	46.4	12.8
Control	4,763	3,738	14.5	3,348	10.4	76.5



A *B*

Fig. 7. Silkworm caterpillars showing mosaicism induced by irradiation of the paternal sperm. *A*, dark caterpillars show characters of the paternal strain and light show characters of maternal strain; *B*, first generation offspring of irradiated father showing mosaicism. (From Astaurow, 1937.)

Another factor which should be taken into consideration is that there is no difference between somatic cells and germ cells as far as genic content is concerned. As a rule, all living cells of an organism possess a full complement of genes. Therefore, similar changes in the heredity-bearing material may occur both in germ cells and in somatic cells.

In attempting to interpret the evidence which shows that flies taken from two stocks of *Drosophila* were differentially affected by the same irradiation, it is well to keep the two facts just mentioned in mind. This result indicates that genes in one strain are more sensitive to irradiation than the genes of another strain. This difference in sensitivity could not be attributed to a difference between two sets of genes but, rather, to a difference in gene environment. This, in turn, suggests that similarly a difference in gene sensitivity may be expected in different tissues of the same organism. Since changes in heredity-carrying material can readily be induced in somatic tissues and since an appreciable proportion of these changes is lethal to the cell, such a difference in sensitivity would readily explain the differential lethal effect of irradiation in various tissues. This internal difference could account for reactions within the same organism whereby one tissue is injured or killed by a certain intensity of irradiation while another tissue may not show any detrimental effect at all. Similarly, this situation can explain the differential effect of radiation in the treatment of cancerous growth.

On the other hand, the observed differences in sensitivity to irradiation show that biological factors play an important rôle in the effects of x-rays on living organisms. It is evident that different individuals may be sensitive to a different degree to x-rays

and that a dosage which is beneficial for one individual may be injurious to another or may be ineffective for a third. Such differences are expected to be especially frequent in man since cross-breeding, which is generally in force, favors variability among individuals of the human race.

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SURFACE AND DEPTH INTENSITIES FOR SHORT DISTANCE LOW VOLTAGE THERAPY

By M. C. REINHARD *and* H. I. GOODALE, *Buffalo, N. Y.*

From the State Institute for the Study of Malignant Disease, Burton T. Simpson, M.D., Director

RECENTLY several manufacturers have introduced shock-proof x-ray tubes for operation at low voltages (up to 140 kv.p.) for superficial therapy. The enclosing of such a tube in an insulating shell, automatically increases the filtration above that of the glass shell itself, which, with the unprotected type of tube, was the only filtration.

Since this inherent filtration will alter the quality of the beam and also since the shock-proof feature permits the use of shorter target-skin distances, the following measurements were undertaken in order to determine the quality, surface-field size, relationship, and relative depth intensities for such distances as might be used with this type of equipment, namely, 11, 15, and 20 cm. target-skin distances. These data have been assembled in charts, which

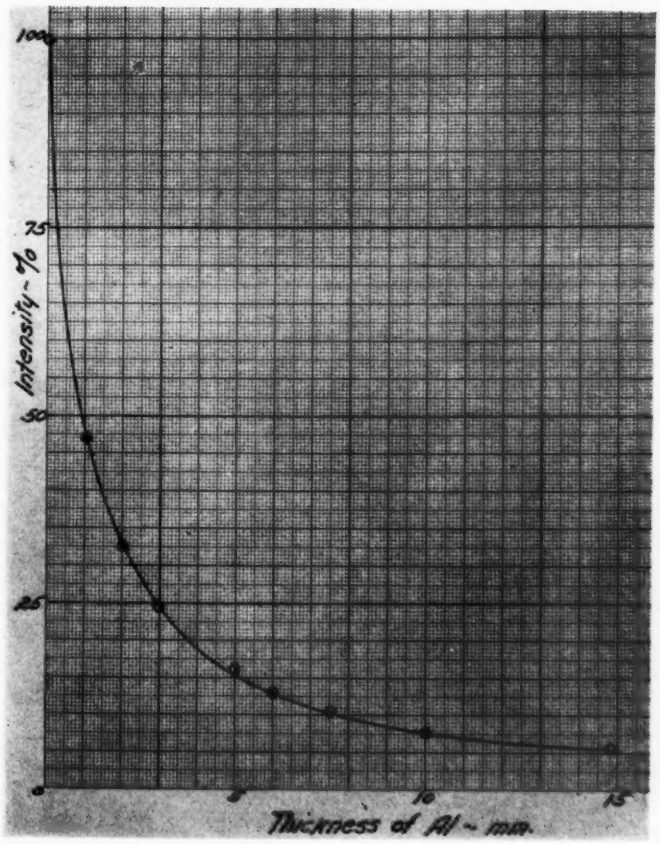

Fig. 1. Aluminum absorption curve—no filter; 100 kv.p. (G. E. Co.), shock-proof tube type SP 1–4.

are useful, not only for these new shock-proof tubes, but also in transition from the old unprotected unfiltered superficial technic to the new type of tubes and treatment.

the density of which was the same as that of water. The x-ray tube was the shock-proof, oil-immersed General Electric X-ray Company tube, type SP 1-4, having

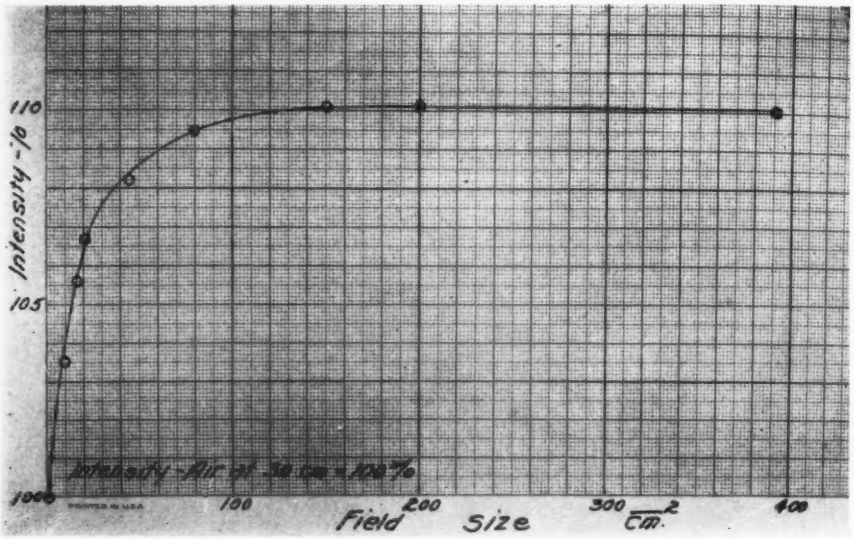

Fig. 2. Back-scatter with various sized fields; half value layer 0.9 mm. aluminum.

For this work all measurements were made with a Victoreen condenser r meter, used in conjunction with a wood phantom, an inherent filter equivalent to 0.5 mm. aluminum.

Quality measurements were first made

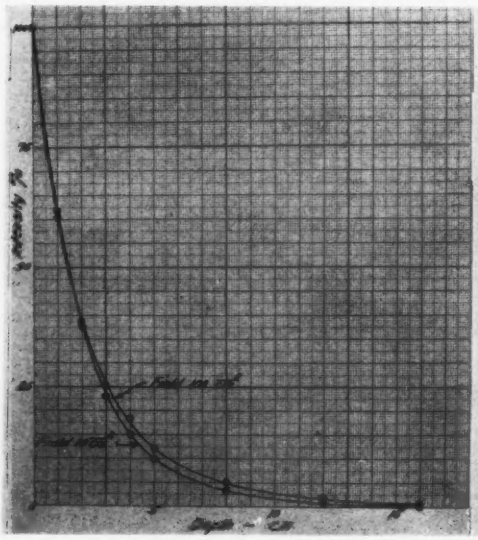

Fig. 3. Depth intensities; distance 11 cm., half value layer 0.9 mm. aluminum.

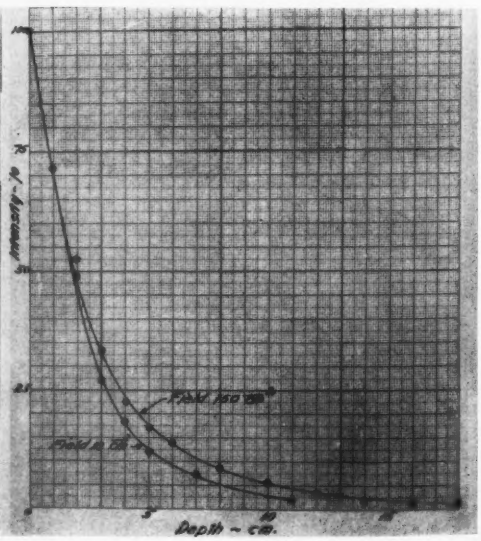

Fig. 4. Depth intensities; distance 15 cm., half value layer 0.9 mm. aluminum.

using aluminum as the absorbing medium. A curve drawn from the data obtained from the aluminum absorption measurements indicates that when this tube is run at 100 kv.p., without additional filter, the half value layer is 0.9 mm. aluminum (Fig. 1). According to the Grebe Nitzge Tabellen, this corresponds to a half value layer of copper of 0.28 mm. and an effective wave length of 0.57 Å. When additional aluminum filtration is used, the approximate quality may be obtained from this curve.

In Figure 2, the relation between intensity and field size is given. The intensity as measured with the ionization chamber free in air is 100 per cent. The intensity measurements made with backscatter from the various fields is related to the air measurements as shown by the curve. We would like to emphasize that this is an intensity curve and not a dosage curve.

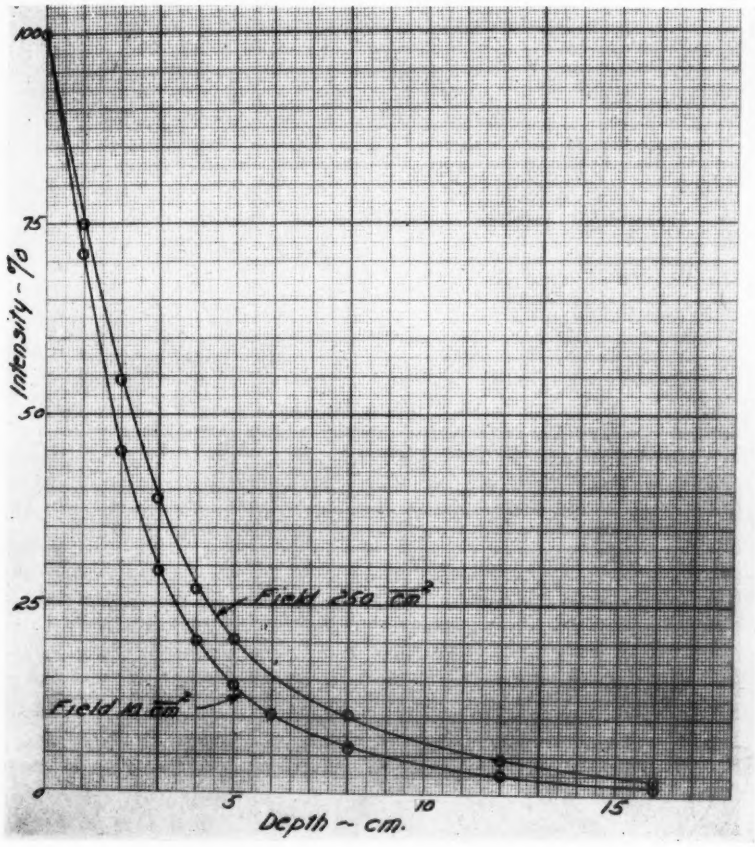

Fig. 5. Depth intensities; distance 20 cm., half value layer 0.9 mm. aluminum.

The intensities for target-skin distances from 11 to 30 cm. were measured with the ionization chamber free in air. The values obtained were compared with calculated values using the inverse square distance law. The agreement between the two was very close, indicating that this law holds also for these shorter distances.

Depth values are given in the following curves (Figs. 3–5) for two field sizes at the three distances. These depth intensities

TABLE I.—DEPTH INTENSITIES

(Half Value Layer = 0.9 mm. Aluminum)

	11 cm. distance		15 cm. distance		20 cm. distance	
Depth (cm.)	Field 100 cm.²	Field 10 cm.²	Field 150 cm.²	Field 10 cm.²	Field 250 cm.²	Field 10 cm.²
0	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%
1	62.25	61.5	71.25	71.3	75.0	71.0
2	39.0	38.5	52.75	48.8	54.3	45.0
3	25.3	23.3	33.25	27.1	38.7	29.25
4	18.0	14.7	22.5	19.0	26.6	20.0
5	12.0	10.0	16.75	12.0	20.2	14.0
6	9.0	6.8	13.8	9.5	15.8	10.25
7	6.75	5.0	10.6	7.0	13.0	8.4
8	5.5	3.7	8.1	5.0	10.75	6.4
9	4.2	2.75	6.75	3.7	8.4	5.0
10	3.25	2.0	5.4	2.5	6.6	3.8
11	2.5	1.5	4.4	1.75	5.25	3.0
12	2.0		3.0		4.5	2.2
13	1.5		2.9		3.5	1.8
14	1.25		2.2		2.9	1.5
15	1.0		1.8		2.0	1.3
16	0.8		1.5		2.0	0.75

are tabulated in chart form in Table I. The field sizes are 10 sq. cm. for a small field and for a large field the maximum spread of the beam is utilized. This last is 100 sq. cm. at 11 cm. distance; 150 sq. cm. at 15 cm. distance, and 250 sq. cm. at 20 cm. distance. The depth intensities for the intermediate field sizes can if necessary be interpolated from these values, although the difference between the curves at the shorter distances is too small to make this necessary.

It is planned to expand this work to include aluminum filtration of various thicknesses.

SUMMARY

Surface and depth intensities are given for a shock-proof x-ray tube operated at 100 kv.p. (half value layer 0.9 mm. aluminum) for the following distances and field sizes:

1. 11 cm. target-skin distance, 10 and 100 sq. cm. fields;
2. 15 cm. target-skin distance, 10 and 150 sq. cm. fields;
3. 20 cm. target-skin distance, 10 and 250 sq. cm. fields.

ADVANCING OSTEOSCLEROSIS OF UNKNOWN ETIOLOGY[1]

ROENTGENOLOGICAL MANIFESTATION OF A PROBABLE INFECTIOUS PROCESS OF THE BONE

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From the Roentgen-ray Department of the University Hospitals

THE number of cases of osteosclerosis reported in the literature is great, and the conditions which lead to bone condensation are also numerous. The earliest cases reported in the roentgenological literature were those produced by metastatic tumors. The term "ivory vertebra" has been utilized for some time to name a vertebral body which casts an intense and homogeneous shadow, with a well maintained form and a normal sized intervertebral space on the roentgenogram and which is so commonly seen in prostatic metastases. Carcinoma of the breast has been also known to lead occasionally to osteoplastic metastases, although the osteoclastic form is more usual in this condition.

Hodgkin's disease is another condition in which osteoplastic bone changes occur, at times mainly in the pelvic bones and vertebræ. Hultén (8) reported the roentgenological finding of several compact, structureless vertebral bodies with well maintained form and contour, in a patient suffering with Hodgkin's disease. Fraenkel (5) similarly observed a case of Hodgkin's disease in which all the long bones showed an extensive, generalized ossifying periostitis.

Marble disease, a systemic condition first described by Albers-Schönberg (1), forms another group, in which the roentgenogram shows a generalized osteosclerosis, represented by an almost complete obliteration of the medullary portion and a marked thickening of the cortex of all the flat and long bones.

In osteopoikilosis, described independently by Albers-Schönberg (2) and Ledoux-Lebard and Chabaneix (10), the roentgenogram showed all the bones to be studded by innumerable, spherical areas of structureless condensation, generally measuring between three and eight millimeters in diameter.

The literature contains many cases in which, in connection with diseases of the blood, sclerotic changes occurred in the bones. Heuck (6) was the first to describe osteosclerotic changes in leukemia. Nauwerck and Moritz (12) demonstrated the simultaneous occurrence of osteosclerosis and atypical leukemia, while Reiche (14) found it in a case of aleukemic myelosis. Assmann (3) described generalized osteosclerosis in three cases of anemia and concluded that the osteosclerosis was related to the generalized disease of the blood-forming apparatus. Overgaard (13) made similar observations in a woman 41 years of age. Hirsch (7) reported a case of generalized osteosclerosis associated with essential polycythemia.

Paget's disease most commonly leads to a marked widening of the bones with rearrangement of the bone trabeculæ in a fasciculated or mosaic-like fashion and to a thickening of the individual trabecula. Occasionally, however, Paget's disease may lead to the formation of dense, structureless bones. Jaffe (9) reported a case in which the gross appearance of the specimens showed zones of intense sclerosis without thickening of the bone, so that Paget's disease was nowhere suggested. Only the microscopical appearance revealed the true nature of the disease.

Moller and Gudjonsson (11), in 1932, described another condensing osteitis hitherto unknown to occur in humans. This condition was proven to be due to fluorine poisoning and was discovered among many employees of a factory who were exposed to cryolite dust. The bones of the thorax

[1] Presented before the Fifth International Congress of Radiology in Chicago, Sept. 13–17, 1937.

vertebræ, pelvis, and of the extremities showed on the roentgenogram a more or less marked condensation, the normal osseous structure having been replaced by a milky white opacity.

Finally, there is a group of sclerotic osteitis of unknown etiology. Sicard, Gally, and Haguenau (16) were the first to use this term in 1926. They reported five cases of condensing osteitis. However, these authors' patients were not carefully studied. Only one examination was performed in each case; there were no histological studies, and the period of observation was short, amounting to two or three months only. On studying the reproductions of their cases, one gains the impression that with the exception of one case, all of them could have been due to metastatic tumors.

Bársony and Polgár (4), in 1928, reported a condition described by them as ostitis condensans ilii. They observed several patients in each of whom the ilium showed a localized sclerosis in the neighborhood of the sacro-iliac joint. The authors were unable to perform serial examinations and were likewise unable to determine the etiological factor in their cases.

Rendich and Shapiro (15), in 1936, reported 12 cases, in which the roentgenologic findings were identical with the cases reported by Bársony and Polgár. Some of their patients presented clinical symptoms, usually of the low back pain type. The disease was found to occur in both sexes. The examination of the entire osseous system failed to show evidence of multiplicity, except that occasionally the opposite ilium was also found to be involved. In one of the cases, during an operation for sacro-iliac fusion, a piece of bone was removed for histological examination and the changes were found to be due to an inflammatory process. The author concluded that the disease did not fall within the category of the known bone diseases, the etiology and the pathogenesis of the condition was unknown, and its clinical significance was debatable.

The present report is concerned with a case in which progressive sclerotic bone changes occurred in the pelvic bones, vertebræ, and scapulæ associated with mild clinical symptoms. The patient had been under observation for almost six years and in spite of careful clinical roentgenological, microscopical, and chemical study, no definite conclusions could be reached concerning the nature of the condition. The lesions to be discussed subsequently do not bear any resemblance to any of the hitherto described bone lesions of either known or unknown etiology.

R. W., a colored male, entered the University Hospitals in October, 1924, when he was 16 years of age. Following an attack of sore throat and migratory multiple joint pains, he developed a pericarditis and endocarditis. Pericardiectomy was done and 450 c.c. of reddish-brown fluid was removed. The fluid contained pneumococci. His general condition improved, but a hypertrophy of the left heart and a systolic and diastolic murmur remained stationary. In 1931, at the age of 21 years, he registered at the Out-patient Department because of pain at night—only in his back and left knee. X-ray examination at this time showed areas of bone sclerosis scattered throughout the upper portions of both ilia, the sacrum, and the lumbodorsal vertebræ which simulated the appearance of prostatic metastatic tumors.

The dull, aching bone pains persisted until the next admission in September, 1934. A few days before this admission, the patient was seized with a sudden pain in the back of his head and neck. Lumbar puncture was done and it showed a pressure of 450 mm. of water, normal dynamics, and grossly bloody fluid. The fluid was not xanthochromic. Wassermann and gum mastic tests were negative. The diagnosis of spontaneous subarachnoid hemorrhage was made. During his stay in the hospital he developed severe pain in both wrists which responded to amydopyrine. The systolic and diastolic murmurs over the aortic area were still present. Repeated calcium and phosphorus determinations

of the blood were normal. Phosphatase ranged around 20 units (Bodansky). The red blood count varied between 4,850,000 and 4,000,000, with the hemoglobin varying correspondingly between 85 and 70 per cent and the white count from 12,000 to 8,500. The sedimentation rate was rapid, varying on different occasions between 1.5 mm. and 0.9 mm. per minute. The urine examination was negative. The development of rheumatic joints during his hospital stay suggested the fact that rheumatic fever played an important part in the subarachnoid hemorrhage. The roentgenological examination showed the sclerotic bone changes to have progressed. The back pain still persisted. The patient left the hospital 63 days after admission—improved.

He was re-admitted on Feb. 18, 1936. Examination showed that extremes of motion in the cervical vertebræ were painful; however, there was very little limitation. He stood in good posture, with no increase in his dorsal and lumbar curves. The legs were equal in length. All motions of his legs and hips were normal. There was a moderate limitation of forward and backward bending. Repeated calcium, phosphorus, and phosphatase determinations were again normal. The blood Wassermann and Kahn's precipitation tests were negative.

On Feb. 20, 1936, a piece of bone approximately 1.5×1.5×1.0 cm. was removed from the crest of the right ilium. The piece was very firm and was composed of pale red cancellous bone. The microscopical sections, described by Dr. Harry Goldblatt, were composed of compact spongy bone with trabeculæ that were thick, irregular, and well calcified. Some of these trabeculæ showed definite parallel lamination, but no signs of mosaic formation. A single layer of osteoblasts was present around most of the trabeculæ. In the spaces between the trabeculæ there were only a few islands of normal bone marrow. The bone marrow was replaced by fibrous connective tissue which was either richly cellular and dense or poorly cellular and edematous. In addition, in many of the spaces there were granulomatous inflammatory lesions, which consisted mainly of foci of epitheloid cells, within which, or surrounding which, were giant cells of the Langhans type. In the sections of one piece of tissue there was a zone of recent hemorrhage, in the immediate neighborhood of which some of the trabeculæ showed degenerative changes and necrosis. Most of the trabeculæ were well preserved and the nuclei of the bone cells stained quite distinctly. Special stains for tubercle bacilli failed to reveal any acid-fast or other micro-organisms in the granulomatous lesions. The diagnosis of osteosclerosis with granulomatous myelitis, possibly tuberculous, was made.

The chemical analysis of the piece of bone, together with some bone marrow, showed its water content to be 10.96 per cent. The normal water content of bone free of bone marrow is between 20 and 25 per cent, consequently the specimen contained less than one-half of the normal amount. The ash content was 59.5 per cent (normal about 40 to 45 per cent), an increase of about 15 to 20 per cent. The calcium content of the ash amounted to 41.7 per cent and the phosphorus 18.65 per cent, which is an approximately normal figure and ratio. The fluorine content was 0.035 per cent (normal 0.035 to 0.065 per cent).

The patient was re-admitted for further study on Dec. 5, 1936. Since his last discharge he had been wearing a back brace, which relieved his back pain to a great extent, but with a fairly marked stiffness and limitation of motion. The red blood cell count was 4,100,000 and the hemoglobin 78 per cent. The blood calcium, phosphorus, and phosphatase figures were within normal limits again.

ROENTGEN-RAY STUDIES OF THE BONES

Pelvic Bones and Upper Femora (Oct. 18, 1931, and Jan. 21, 1932).—Scattered throughout both iliac bones there are many circular areas of bone condensation.

Fig. 1. Taken on Oct. 8, 1931, this film shows rather sharply defined circular and oval areas of condensation scattered throughout the pelvic bones.

The normal architecture of the bone is either completely obliterated or indistinct throughout these areas. The trabeculæ show a marked thickening and the intertrabecular spaces are either absent or markedly narrowed. The circular areas measure between 2 and 3 cm. in diameter, the oval ones 1.5×2 to 2.5×5 cm. In the medial portion of the right ilium, near the sacro-iliac joint, several of the circular areas are confluent.

The contours of the areas of condensation show a fine fuzziness, but otherwise they are sharply demarcated from the neighboring normal osseous structures. The central portion of the sacrum shows an oblong area of condensing lesion measuring 7 cm. in length and 4 cm. in width. The ischium and pubic bones likewise show oblong areas of condensing lesion. The sacro-iliac and hip joints appear to be normal (Fig. 1).

Vertebral Column.—There is an extensive sclerosing process involving the lower six dorsal and all the lumbar vertebræ. Some of the sclerotic areas are circular, but are not as sharply demonstrated as those of the pelvic bones. The sclerosis of the

Fig. 2. The lumbar vertebræ also show scattered areas of condensation, which are irregularly defined.

Fig. 3. Lateral view of lumbar vertebræ demonstrating the areas of bone condensation. The contours of the vertebral bodies are normal.

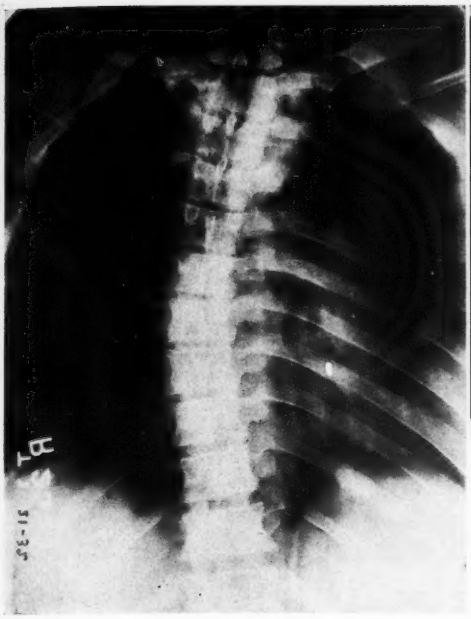

Fig. 4. Shows the appearance of the condensating areas in the dorsal vertebræ.

eleventh and twelfth dorsal and the first lumbar vertebræ involves uniformly the entire vertebral bodies. The upper six dorsal and the cervical vertebræ show a similar, but less marked, change. Neither the arches nor the spinous or transverse processes are involved. The small intervertebral joints and the intervertebral spaces are normal (Figs. 2, 3, and 4).

The ribs, clavicles, and the bones of the skull show no abnormalities.

Humeri and Scapulæ.—The necks of the scapulæ show some diffuse, but not extensive condensing lesion (Fig. 5). The humeri are normal.

The sclerotic process throughout the pelvic bones (examinations Oct. 3, 1934, and Jan. 10, 1935) has become generalized and the dense areas have become confluent. Only the central portions of the ilia and the distal end of the sacrum show normal architecture. The condensing lesion of the vertebral bodies has likewise progressed; they are uniform in density and ivory-like. The cervical vertebræ are also involved (Fig. 6). The configuration

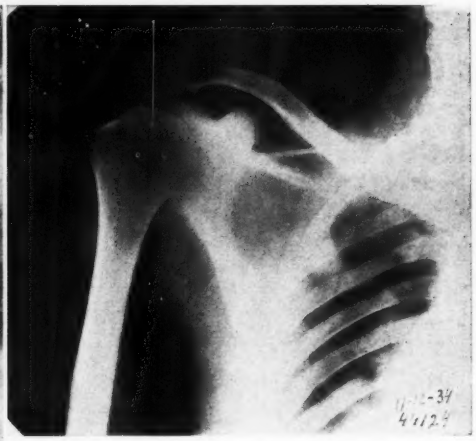

Fig. 5. The neck of the scapula shows a marked sclerosis.

of the pelvic bones and vertebræ are well maintained despite the marked structural changes. The cervical vertebræ and the necks of the scapulæ are also denser than before.

The appearance of the pelvic bones and vertebræ on Nov. 5, 1935, remains unchanged. Several additional long bones were examined and were found to be normal.

The sclerotic bone changes, as observed Nov. 20, 1936, have progressed slightly (Figs. 8 and 9).

DISCUSSION

The changes found in this patient's bones are unusual. The initial examination showed circular and oval areas of condensing lesions in the pelvic bones and vertebræ in a 21-year-old colored individual. They were suggestive of metastatic tumors of the type seen in prostatic carcinoma. However, the patient's age and the normal appearance of the prostate did not seem to justify this diagnosis. During an observation period of almost six years, the well demarcated lesions became confluent, leading to a generalized condensation of ivory density of all the involved bones, with well maintained contours and forms. Among the remaining bones only the necks of the scapulæ

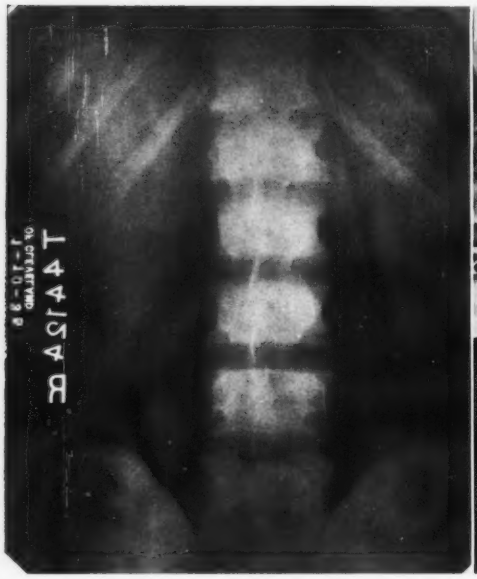

Fig. 6. Anteroposterior view of the lumbar vertebræ taken three years after the first examination, showing the sclerosis of the vertebral bodies to have become uniform

Fig. 7. The sclerosis extends into the cervical vertebral bodies.

showed some condensation. The patient's clinical condition remained very good, and the only symptom referable to the bone lesion was an intermittent dull, aching pain in the back with practically no disability.

The biopsy of the bone showed a thickening of the bone trabeculæ with a granulomatous myelitis suggesting tuberculosis, yet no tubercle bacilli were found in any of the sections. Consequently, the microscopical examination failed to give full information as far as the etiology of the disease was concerned.

The chemical analysis showed only increased ash content and diminished water content, but otherwise normal composition. It helped to rule out fluorine poisoning.

Despite the severe osteosclerosis of many of the flat bones, the blood picture remained relatively normal. Apparently the normal bone marrow of the uninvolved bones was still able to compensate for the loss of the blood-forming spaces in the diseased bones. The approximately normal blood picture likewise enabled one to eliminate a bone disease associated with blood dyscrasias. Syphilis of the bones had been ruled out by the repeatedly negative spinal fluid and blood Wassermann and Kahn precipitation tests. There were no clinical manifestations to indicate the presence of Hodgkin's disease. Metastatic tumors and Paget's disease were eliminated by the microscopic study and the clinical course. Neither the roentgenological appearance, the blood chemistry, nor the histological examination indicated the presence of hyperparathyroidism.

Apparently the disease represents a low grade bone infection either of tuberculous or pyogenic etiology. It probably belongs in the same group of cases which were reported by Bársony and Polgár, and subsequently by Rendich and Shapiro. Yet in their cases, the roentgenological manifestations are quite different, the disease being localized to the medial portion of the ilium.

As far as tuberculosis is concerned, there is nothing in the patient's clinical history and symptomatology to indicate the presence of this condition. The lung-fields are

Fig. 8. Film of pelvis taken five years after the first examination shows that the sharply defined areas of condensation have become confluent. Only the central portions of the ilia remain unsclerosed.

clear, and roentgen-ray examination of the abdomen shows no evidence of calcified mesenteric or retroperitoneal nodes.

On the other hand, there is ample evidence in the patient's clinical history of previous non-tuberculous infections. He had a septic pericarditis in 1924, which necessitated surgical intervention. The patient suffers from an aortic and mitral valvular disease, and there is a history of repeated rheumatic involvements of several small joints. There is likewise a history of a spontaneous subarachnoid hemorrhage which clinically was thought to be rheumatic in origin.

There is a possibility that through bacterial embolism with slightly virulent micro-organisms a low grade infectious process was originated in the involved bones, leading to a secondary condensing lesion, without evidence of suppuration.

We are presenting this case to the members of the International Congress in the hope that someone may help to elucidate the true nature of the disease.

Fig. 9. Lateral view of the lumbar vertebræ five years after the first examination. The vertebral bodies are ivory-like in density. The vertebral contours and intervertebral spaces are normal.

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NEUROBLASTOMA: A CHILDHOOD TYPE OF MALIGNANT TUMOR OF THE SYMPATHETIC NERVOUS SYSTEM

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THE fact that we have encountered two cases of neuroblastoma, a comparatively rare disease, within a period of one year, has prompted us to report these cases and, in addition, to review some of the literature dealing with this fascinating subject.

Definition.—Neuroblastoma can be defined as a malignant tumor, derived from neuroblasts. However, this statement conveys no significant impression unless one is familiar with the embryonic stages in the cellular development of the nervous system.

Embryology.—The medullary epithelium is formed of primitive undifferentiated nerve cells of ectodermal origin. Early in the course of histogenesis of the nervous system, these cells lining the medullary groove differentiate themselves into two main divisions—*germ cells* and *spongioblasts* (Fig. 1).

The germ cell in turn gives rise to two types of cells, the neuroblast and the medulloblast. The neuroblast ultimately becomes the neuron or adult nerve cell. Both the neuroblast and the neuron have an affinity for silver (which fact is utilized to advantage for identification by means of this staining selective property). The neuroblasts are not only the precursors of neurons but also give rise to migrating cells (springing from ganglionic cells), the anlage of the sympathetic nervous system. Some of the neuroblasts migrate ventrally toward the aorta to form the sympathetic chains and the chromaffin paraganglionic structures, and also invade the mesodermal part of the suprarenal gland to form the chromaffin and ganglion tissue of the medulla (19). The medulloblast has no affinity for silver or gold. It is believed that the medulloblast can develop into a spongioblast or a neuroblast, or may give rise to an adult type of neurogliar cell called oligodendroglia.

The other main cellular division of the medullary epithelium manifests itself as spongioblasts. During the process of maturation these cells pass through the ripening phases of astroblasts, protoplasmic, and fibrillary astrocytes, and finally become the adult glia or neuroglia cell which is the important supportive cellular structure of the central nervous system. These elements stain with gold impregnation methods.

Gliomas are derived from glia or neuroglia cells, and are the common tumors of the central nervous system. For some unexplained reason, the primitive neuron elements are more apt to exist in the sympathetic nervous system than in the central nervous system, and so neuroblastomas are more generally found in the sympathetic chains and in the adrenal cortex, more frequently in the latter.

Study of Figure 1 will be of great aid in visualizing the transitional stages of the cellular development of the nervous system, and the specific type of tumor derived from each of these cells. This schematic chart has been formulated from composite data derived from literature published by Bailey (1) and Boyd (2).

Pathology.—In the older literature, neuroblastoma of the adrenal was mistaken for sarcoma because of the soft cellular sarcoma-like appearance of the tumor tissue. It was Virchow, in 1864, who first guessed at the nervous tissue origin of these congenital suprarenal tumors, but he regarded them as gliomas. Küster (12), Lapointe and Lecéne (13) reported tumors composed of undifferentiated sympathetic cells as gliomas of the adrenal, believing the rosettes were embryonic misplaced glia tissue. Wright (23), in 1910, was the first to properly name the tumor as "neuroblastoma." Quoting him—

"Histologically the tumor is very cellular, resembling primitive migrating cells of the sym-

pathetic nervous system, somewhat larger than a lymphocyte, with a densely chromatic nucleus, and a narrow rim of cytoplasm. The

Clinical Picture.—Neuroblastoma generally occurs during infancy or childhood and is exceedingly malignant. In the

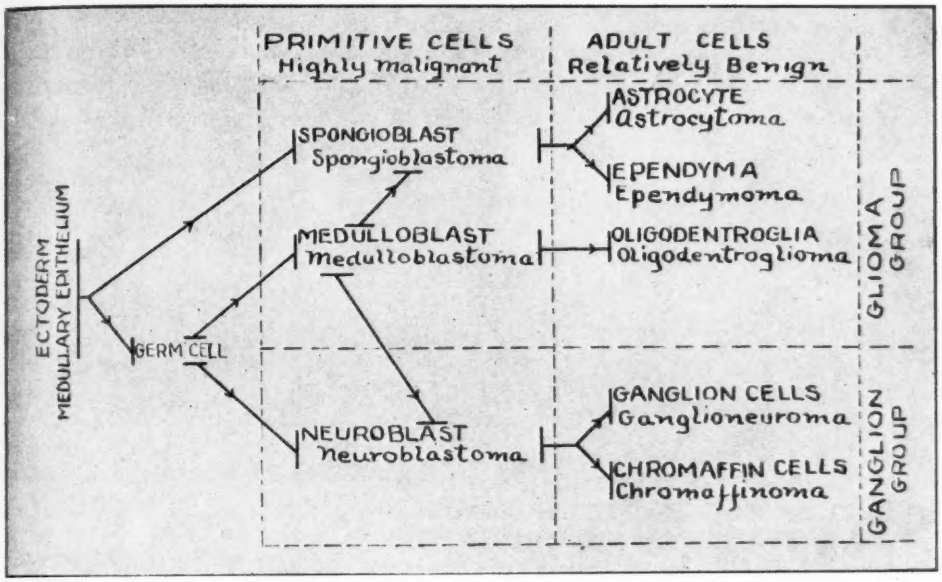

Fig. 1. Schematic chart of cellular development of nervous system and the type of tumor derived from each of these cells.

matrix in which the cells rest contains delicate fibrillæ which do not take the stain of connective tissue, collagen, or neuroglia. They are probably primitive axis cylinders. The cells often assume a roughly circular formation about a bundle of fibrillæ. These characteristic tumor 'rosettes' are found in the primary tumor but not usually in the metastasis."

It must be remembered that in the biopsy study, rosettes are seen only in the minority of cases. Lewis and Geschickter (16), in their study of 40 cases, reported the presence of rosette formation in only one-third of their group. In the absence of rosettes, an absolute diagnosis from the pathologic specimen alone is often exceedingly difficult and occasionally impossible. Rypins (20) emphasizes the fact that since the characteristic finding is a small round cell, highly undifferentiated, with a considerable amount of fibrillar material, the condition is often confused with Ewing's tumor and other highly undifferentiated neoplasms.

adult it is extremely rare. Ritter (19) has reported two cases in persons past middle age, occurring in the intestines, with metastasis to the adjacent mesenteric lymph nodes. Both cases, however, were of relatively benign character. Boyd (2) believes a diagnosis of neuroblastoma in an adult is an extremely risky one.

With the publication of an article by Pepper (18), in 1901, and one by Hutchinson (8), in 1907, each describing a different clinical manifestation of this disease, two types have since been universally accepted, each named after the respective author. In the Pepper syndrome, the tumor starts in the suprarenal, more frequently on the right side, with metastasis to the liver and adjacent lymph nodes. The liver may become so enlarged as to fill the greater part of the abdomen, usually not associated with any jaundice. In the Hutchinson type, there occurs metastasis to the skull, particularly the or-

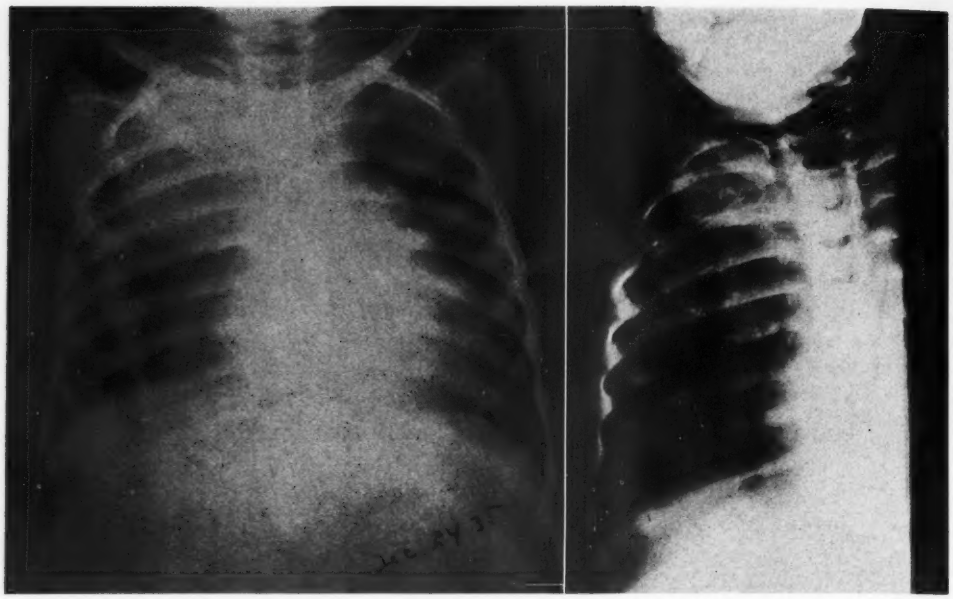

Fig. 2. Case 1. (*Left*) Lung tumor in right upper chest. (*Right*) Right upper chest over-penetrated to demonstrate partial calcific infiltration of tumor.

bital region, and to other osseous structures. There is generally first noticed an ecchymotic spot about one eye, followed later by unilateral exophthalmos, with tumefaction of the temporal region. The abdominal findings generally are of a minor character. The orbital involvement is more apt to occur on the same side as the primary adrenal tumor. Sturtevant and Kelly (21) emphasize the fact that ecchymosis of the eyelids and proptosis, occurring in infants or children, should arouse suspicion of metastasis from a suprarenal growth.

The age group frequently determines the type of syndrome, those in the Pepper class existing more frequently during the infantile stage and the Hutchinson type is more apt to be found during the childhood period. Many cases have been reported in recent years that do not seem to fit into either the Hutchinson or Pepper type. Frequently there are no ocular findings, and the primary tumor does not always occur in the suprarenal structure, as in Case 1, reported in this communication.

X-ray Findings.—Only when there is metastasis to the osseous system can neuroblastoma be suspected or recognized roentgenologically. The tumor generally invades the skull, pelvis, and long bones. The exophthalmos is produced by metastasis in the region of the orbit. The skull findings are generally characteristic (Fig. 3, Case 1). Numerous pin-hole vacuolated areas are seen in the frontal region and to a lesser extent in the entire vault. The cranium frequently has a moth-eaten appearance. Thinning of the cortex is often present, with gaping of suture spaces (9). The shafts of the long bones and the flat bones exhibit small areas of resorption. Periosteal reaction changes in the form of "perpendicular striations," "spicules," and "whiskers" have been described by Henle (6), Lewis (15), Tidswell and Sear (22), Lederer (14), Klein (11), and Rypins (20). Geschickter and Copeland (3), on the contrary, state that periosteal new bone formation is unusual in neuroblastoma.

Radiation Therapy.—Boyd (2), Kwarten and Twiss (10), and Holmes and Dresser

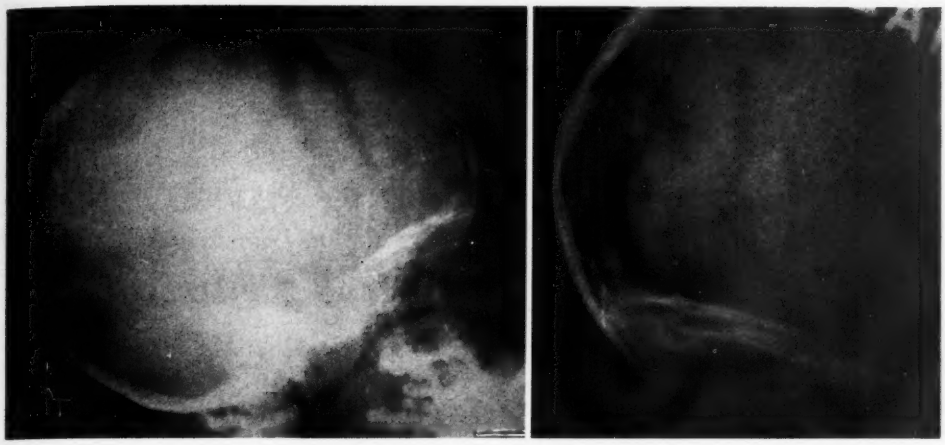

Fig. 3. Case 1. (*Left*) Pin-hole shadow in frontal region of skull with widening of coronal suture. (*Right*) Frontal area magnified for better visualization of minute osteoporotic shadows.

(7) have used radiation therapy in their cases and found that the reaction did not alter the progress of the disease. Gibson (4) states that in inoperable cases, deep roentgen-ray therapy deserves a trial although no statistics are available as to its efficiency. Hauser (5) reports a case which was radioresponsive although only temporarily so. Only x-ray therapy was utilized by us in the two cases recorded in this paper but with very little effect. Apparently the character of response of neuroblastoma metastasis to radiation is similar to that of carcinoma metastasis.

CASE REPORTS

Case 1. D. M., colored, aged 3, admitted on Dec. 10, 1935, to the Queensboro Contagion Hospital as a suspected poliomyelitis. The onset had been insidious, dating back approximately four months prior to admission. There was complete loss of sensation and paralysis was present below the level of the fifth dorsal vertebra. The liver and spleen were not palpable, but the abdomen was moderately distended with gas and sensitive to palpation. Temperature was 104° at the time of admission. X-ray examination of chest (Fig. 2) disclosed a large globular, partly calcified tumor mass in the right upper lobe. It was then considered highly probable that the paralysis of the lower extremities was being caused by pressure on the cord by tumor tissue. A tentative diagnosis of transverse myelitis was made, and the patient transferred to the Queens General Hospital.

All of the osseous structures were then x-rayed. The skull disclosed (Fig. 3) pin-hole vacuolated areas in the vault, chiefly in the frontal region. The coronal suture was separated. The long bones (Fig. 4) showed poorly demarcated osteolytic areas, intramedullary in situation. The areas of bone destruction were larger in the pelvic bones (Fig. 5-*A*). The only sign of periosteal reaction in the long bones was located in the distal fourth of the shaft of the left femur at the external margin (Fig. 5-*B*). Roentgenologically a diagnosis of "probable neuroblastoma" was made.

Blood Study.—Urea nitrogen, 60.3 mgm.; cholesterol, 312 mgm.; Wassermann and Kline tests negative. Blood culture positive for *Staphylococcus albus*. Hemoglobin, 30 per cent; red blood corpuscles, 2,290,500; white blood corpuscles, 7,520; 61 per cent polymorphonuclears; 32 per cent lymphocytes; 6 per cent monocytes; 1 per cent eosinophiles.

Urine Examination.—Negative except for trace of albumin.

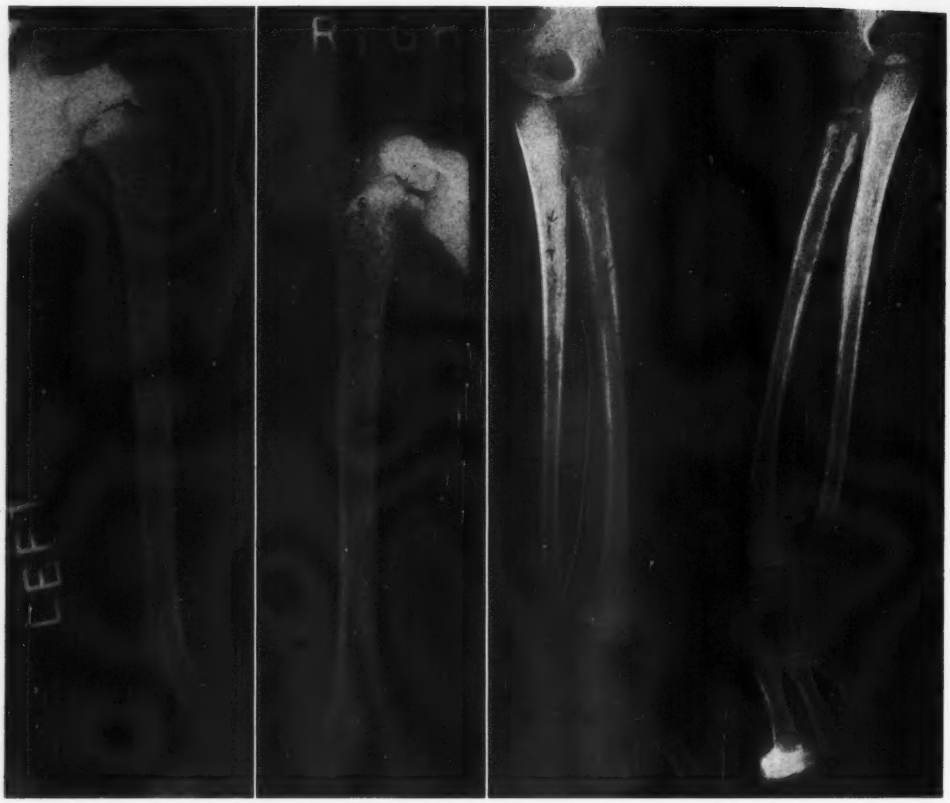

Fig. 4. Case 1. (*Left*) Intramedullary osteolytic areas in shaft of left humerus, and punched-out zone of bone destruction at proximal end of diaphysis of right humerus externally. (*Right*) Intramedullary rarefying areas in radius and ulnal bones, with partial destruction at proximal end of diaphysis of each radius externally.

Physical status of the patient remained approximately the same for about ten days, after which he became progressively worse. Transfusion was given. On December 25, a hard irregular glandular mass was discovered in the right inguinal region. Biopsy report of inguinal lymph nodes follows.

"*Gross description:* Specimen consists of four portions of tissue and consists of several discrete lymph nodes. One portion measures 20 × 10 × 15 mm.; the other three particles measure approximately 5 mm. in diameter and are discrete. A whitish tissue is noted on section, with no distinct architecture.

"*Microscopic description* (Fig. 6): Section shows delimited area of cellular tumor tissue with hyperchromatic but rather uniform nuclei, with distinct trabeculated, lobulated, and alveolar structure. Distinct fibrils can be made out in association with some of the cells. No distinct characteristic rosettes are evident in the section. Some areas of necrosis and some vascular invasion and extension are noted. Lymph node structure is lost in most of the section. In one fragment sinusoids are found filled with hyperchromatic tumor tissue, with intervening thin columns of lymphoid stroma.

"*Pathological diagnosis:* Malignant infiltrating tumor suggesting neuroblastoma."—A. Angrist.

Four x-ray high voltage treatments were given over the dorsal spine and three over the right anterior chest, each treatment consisting of 100 r units. No beneficial effect was noted.

The child became weaker, with tempera-

ture varying between 98.8 and 106.4 degrees. The pulse range was between 100 and 140, and respirations between 24 and 48. On January 21, a transfusion of 100 c.c. was given. The patient died on January 27.

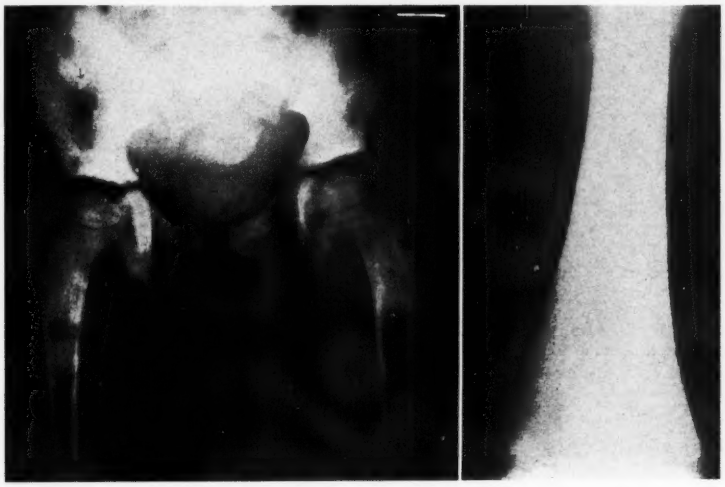

Fig 5. Case 1. (*Left*) Large poorly demarcated osteolytic areas in pelvis and upper femora. (*Right*) Periosteal elevation (magnified) at margin of lower femur.

Postmortem Record.—Autopsy Jan. 27, 1936. Pathologists, Dr. Santora and Dr. Davidson. Limited examination only.

Anatomical Diagnosis

1. Neuroblastoma of upper sympathetic ganglion, with
2. Massive metastasis to lymph nodes;
3. Metastasis to bone;
4. Extensive lymphatic and blood vessel permeation;
5. Transverse myelitis in cervical region by compression through vertebral bodies (clinical);
6. Cystitis;
7. Secondary anemia, marked;
8. Pulmonary edema, marked.

Cause of Death.—Neuroblastoma with extension and cord compression and terminal ascending infection.

Microscopic Examinations (tumor tissue).—Extensive necrosis and large groups of hyperchromatic cells with some fibrillar tissue. Most of the cells are small and rounded, with scant cytoplasm. There is an area quite large and hyperchromatic. Definite extension into lymphatic and vascular channels is evident. Some cells show ganglion cellular characteristics with distinct nucleoli and considerable cytoplasm. Other cells show considerable lipoid accumulation in the cytoplasm. A rare rosette structure can be made out. Bielschowsky stains show some cellular positive fibers in direct relationship to groups of cells. Fibers are prominent and numerous and suggest that the fibrillar background noted in the hemotoxin and eosin sections are in part neurofibrils.

No marked changes or significant findings disclosed in adrenals, kidneys, liver, or spleen.

Case 2. L. F., aged three and one-half years, white female, admitted to Trinity Hospital on June 16, 1935, with chief complaints of (1) pain in the upper abdomen with vomiting of four days' duration; (2) mass in upper abdomen; (3) abnormal growth of right leg since infancy.

Past History.—At the age of two months, the child had pyelitis. When five months old, her mother noticed that the baby's right ankle was "swollen." X-ray examination at the Hospital for Joint Dis-

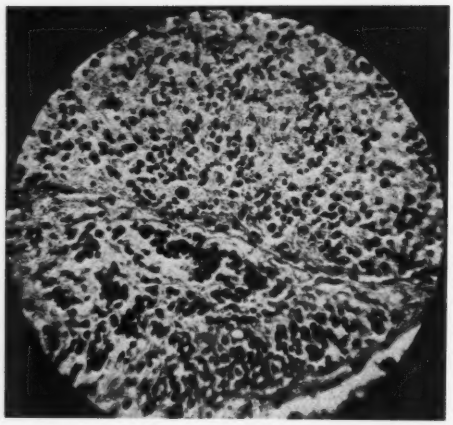

Fig. 6. Case 1. Photomicrograph of section from inguinal lymph node.

eases, May 23, 1932, reported "hereditary deforming chondrodystrophy." The opinion rendered on subsequent roentgenograms, dated April 24, 1933, was that of Ollier's disease. On Feb. 19, 1934, the child developed enlarged cervical glands. X-ray treatments were given over the neck area at St. Mary's Hospital, Brooklyn, in fractional doses over a period of one month to reduce the size of these glands, and also for possible beneficial effect on the bony lesions in the right leg if the same was caused by hyperparathyroidism. Soon thereafter, the child was under observation at the House of St. Giles the Cripple, at which institution a diagnosis of congenital hypertrophy of the right leg was made. Abdominal examination at that time did not reveal any palpable masses or enlarged liver or spleen. On April 15, 1935, patient had the first attack of abdominal pain with vomiting.

Present Complaint.—Recurrence of pain in abdomen, with vomiting for past four days.

Physical Examination.—Well nourished, pale looking child. Head, nose, ears and throat essentially negative. Glands in neck slightly enlarged. Chest negative. Abdomen showed bulging in left upper quadrant. No rigidity or tenderness present. A mass the size of a grapefruit

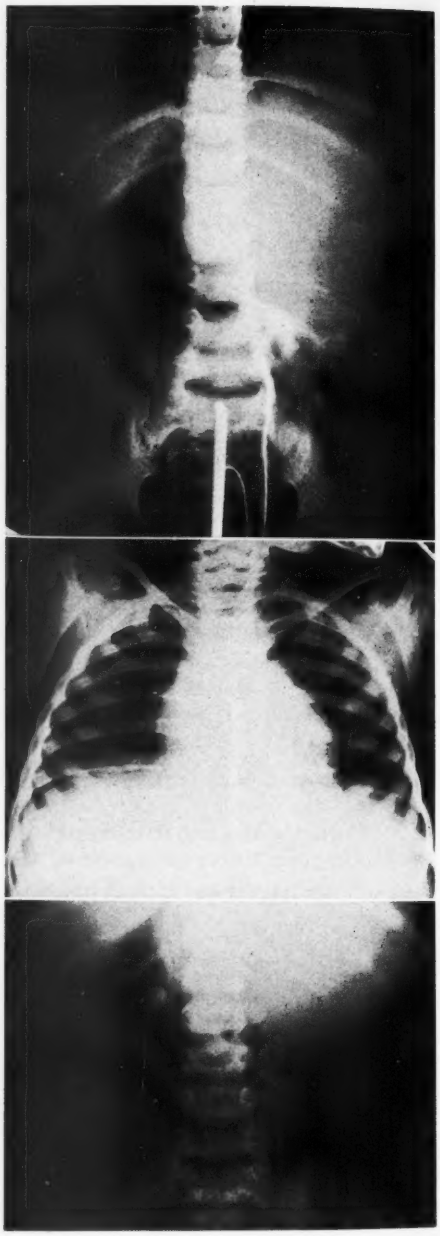

Fig. 7. (*Upper*). Case 2. Left retrograde urography Tumor mass in left upper quadrant with downward displacement and flattening of left kidney pelvis and its calices.

Fig. 8. (*Middle*). Case 2. Destruction of inferior angle of right scapula. (*Lower*) Destruction of outer end of right eleventh rib.

was palpable on the left side of the abdomen, extending from the costal margin to the level of the umbilicus. Liver not

Fig. 9. (*Left*) Case 2. Structural changes in phalanges of index and middle fingers and first and second metacarpal bones of right hand. Left hand negative.

Fig. 10. (*Right*) Case 2. Right leg shows intramedullary osteoporosis of proximal and distal thirds of tibial diaphysis, with structural enlargement of distal fourth of tibia. Left leg normal.

palpable. The right leg was enlarged, but no pitting, tenderness, nor sensory disturbances were disclosed. The middle and index fingers of the right hand were enlarged and somewhat deformed.

Blood Findings.—Urea nitrogen, 13 mgm.; cholesterol, 200 mgm.; blood calcium, 12.5 mgm.; blood phosphorus, 3.7 mgm.; Wassermann and Mantoux tests negative; hemoglobin, 70 per cent; red blood corpuscles, 2,300,000; white blood corpuscles, 8,000; polymorphonuclears neut., 57 per cent; polymorphonuclears mature, 52 per cent; polymorphonuclears immature, 5 per cent; lymphocytes, 43 per cent.

X-ray Findings.—Examination of urinary tract (Fig. 7): left side urography shows left kidney to be displaced downward and mesially by a tumor mass above, associated with flattening and distortion of its kidney pelvis and calices. Roentgenography of the skeletal structures discloses osteolytic changes within the inferior angle of the right scapula (Fig. 8-*A*) and in the outer end of the right eleventh rib (Fig. 8-*B*). There are also well demarcated areas of bone destruction with structural thickening of the proximal and middle phalanges of the index finger and all of the phalanges of the middle finger and less conspicuous changes of similar character in the shafts of the first and second metacarpal bones, right hand (Fig. 9). The right tibia (Fig. 10) presents a few rather poorly demarcated intramedullary longitudinal areas of osteoporosis with structural enlargement in the lower third of its diaphysis, and less pronounced intramedullary osteolytic changes in the upper third of the shaft. Skull findings are negative.

X-ray Therapy.—One high voltage treatment given over left upper quadrant amounting to 200 r units. No beneficial effect noticed.

Operative Findings.—A large suprarenal cystic tumor was present, which was dissected free and removed (July 17, 1935). Kidneys appeared normal. A few enlarged retroperitoneal glands were found. Liver, stomach, pancreas, and spleen were normal.

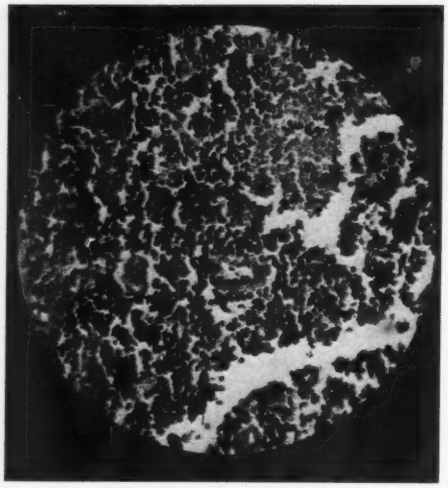

Fig. 11. Case 2. Photomicrograph of section from suprarenal tumor tissue.

Pathologic Report.—"Specimen consists of a cystic mass 12 cm. in diameter. External surface is mottled pearly white and red, rough, slightly lobulated. On section, some of the wall is thinned, but for the most part it is thickened and lined by soft reddish-brown papillomatous material, and some rather fresh blood clot. Microscopic examination [Fig. 11] shows a small amount of loose fibrous tissue stroma to which is attached a tissue composed of a small amount of very fine reticulum supporting numerous small columnar-like cells. This tissue is permeated by numerous delicate blood vessels from the walls of which many of these cells assume a radial disposition. The cells are uniform in size and shape. There are also areas of necrosis and of extensive hemorrhage. An occasional arrangement suggesting rosette formation is seen. Diagnosis: neuroblastoma."—M. Lederer, M.D.

The patient died on the day after the operation.

DISCUSSION

Case 1. It is interesting to note that the primary lesion was in the upper sympathetic ganglia, instead of the more common suprarenal site. Clinically there were no orbital findings such as ecchymosis or unilateral exophthalmos, as is generally seen in the Hutchinson type. The skeletal changes, particularly in the frontal region of the vault of the skull, were sufficient to warrant one in making a roentgenographic diagnosis of "probable neuroblastoma."

Case 2. It is difficult to associate the unilateral skeletal pathology in the right scapula, right hand, right tibia, and right eleventh rib with that of neuroblastoma. The osseous lesions were first discovered three years prior to the disclosure of the suprarenal tumor. Because of the slow growing character of the skeletal changes, one is inclined to believe that the osseous pathology was independent of the neuroblastoma in the suprarenal and that we were dealing with a case of osteodystrophiafibrosa unilateralis, rather than bone metastasis. Unfortunately, no biopsy was obtained of any of the bone lesions.

SUMMARY

1. We have reviewed the embryology, pathology, clinical picture, roentgen findings, and radio-responsiveness of neuroblastoma.

2. Two cases of neuroblastoma have been presented, one in which the primary lesion was located in the upper sympathetic ganglion, and the other in the suprarenal gland.

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CASE REPORTS AND NEW DEVICES

ROTARY STORAGE CONTAINER FOR RADON GLASS CAPILLARIES[1]

By CARL B. BRAESTRUP *and* F. SELLMER,
New York City

From the Physical Laboratory, Division of Cancer, Department of Hospitals

In the Department of Hospitals of the City of New York the emanation plant at the Cancer Institute supplies all the radon for the various municipal hospitals. Since a great variety of radon applicators are used, it necessitates keeping in stock an ample supply of radon glass capillaries.

Fig. 1. Photograph showing unloading of container (actually there is a one-inch lead screen between the container and technician).

In order to protect the radium technicians against stray radiation from the radon in stock, we developed a rotary storage container for the glass capillaries. In the design of this container we had three objects in mind: first, to completely surround the radon tubes with several centimeters of lead; secondly, to reduce the handling of the bare glass tubes to a minimum, and lastly, to develop a method whereby the fragile capillaries were not broken in the process of loading and unloading. The last objective presented the greatest difficulties, but these were finally overcome and the container described herein now has been used for more than a year with no breakage whatsoever.

In Figure 2 is shown a cross-section through the container. Mounted on a vertical shaft is a brass-enclosed cylindrical lead disk provided with 35 compartments, each 32 mm. long and 3 mm. in diameter. The disk which is mounted in a lead-lined brass casing can be rotated around its axis by means of the handle. In the top of the casing is a hole with a funnel through which the capillary tubes may slide into the compartments. By shifting the position of the disk each radon tube is loaded into a separate compartment, the number of which is indicated on a dial at the top.

Each compartment is provided with a trap door at the bottom. This door is normally closed, but may be opened by a lever when the compartment is above the receptacle used in transferring the radon tube to the measuring device or loading table.

In addition to the lead of the container, further protection against stray radiation is obtained by means of a one-inch screen placed between the operators and the container. The device, including the lead screen, is mounted on a truck and may be moved into whichever room it is to be used.

The container is first loaded in the pump room with a capillary just removed from the pump and suitably subdivided, each section being placed in a separate compartment.

The device is later rolled into the measuring room, where each glass tube is temporarily removed from the container to determine its value in millicuries. A record is kept of each capillary, giving the number of millicuries, time of measurement, and the number of its compartment.

The device is finally placed next to the loading bench, where the technician inserts the glass tubes into the various forms of applicators. In selecting the capillary, he consults the above-mentioned record, making correction for the decay of the radon.

To ascertain the amount of stray radiation received by the technicians, we made a series of ionization measurements, using average working conditions.

With nine radon capillaries having a total strength of 174 millicuries, the stray radiation was less than 0.009 r/min. at 30 cm. distance from the center of the container. The calibration of the ionization chamber was obtained by using a 1.98 mg. Ra standard at a distance of one meter. The conversion to roentgens was made by assuming 1 gm. minute = 132 r at a distance of 1 cm., using a filtration of 0.5 mm. Pt. This value checks closely with that ob-

[1] Received for publication, March 2, 1937.

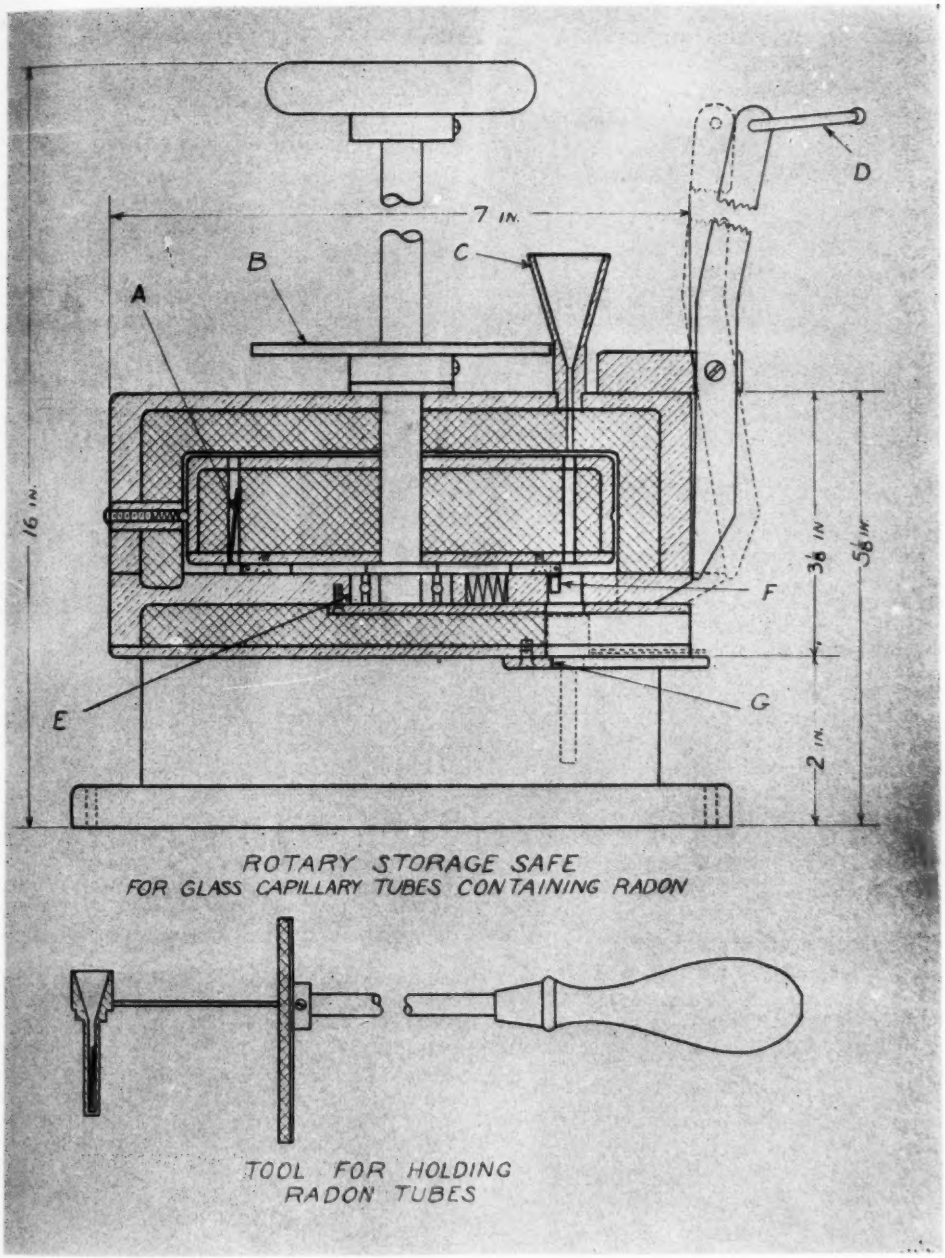

Fig. 2. Cross-section through storage container. Symbols: *A*, radon glass capillary; *B*, dial with numbers for each compartment; *C*, funnel; *D*, lever for releasing trap door; *E*, ball bearing; *F*, trap door; *G*, guide and stop for radon tube holder.

tained by direct x-ray calibration against a standard chamber.

While the storage container in its present form has reduced the stray radiation materially, further improvements are being considered. By rearranging the measuring room, it is plan-

ned to have the storage container remotely controlled, thereby reducing the stray radiation to a negligible amount.

A "BITE-TYPE" SINUS-MASTOID HEAD REST

By J. MARSHALL NEELY, M.D., *Lincoln, Nebraska*

The purpose of this communication is to describe a simple and effective device which permits immobility and accurate position in radiographic study of the paranasal sinuses and mastoid processes. The principle of construction as used for sinus work, is two horizontal bakelite bars which are shaped so as to permit the jaws to clamp over them in both the Caldwell and Waters positions. The board is so built that it fits over an 8 × 10 inch cassette. The horizontal bars are fixed to two upright poles of the correct height to accommodate the mouth in both the Caldwell and Waters positions (Fig. 1). With a minimum of care in positioning the mouth on the bars the sagittal plane of the head is absolutely perpendicular to the plane of the film and it remains only for the tube to be centered in order to obtain perfect position. With the jaws clamped onto these bars it is almost impossible for motion to take place during the exposure. The principle of the mastoid rest is the same, namely, an upright or perpendicular piece which is attached to an adjustable horizontal bar. The upright piece may be moved along the horizontal bar to accommodate the various shapes of patients' heads. The horizontal bar swings from one half of the cassette to the other thereby permitting the exposure of both mastoids on one film (Fig. 2).

In the Waters position the lead cover is removed and the patient is instructed to bite down onto the lower horizontal bar in such a way that the chin and tip of the nose touch the cassette. A piece of good bond paper is placed over the bar for sanitary purposes and between each patient the bar is washed with alcohol or removed and boiled if desired. With the head in this position the tube is tilted from 10 to 15 degrees toward the feet, depending somewhat on the shape of the patient's head, and the exposure to be made (Fig. 3). Since motion is almost impossible the length of exposure is not important and almost any desired combination of technical factors may be used. It is also possible to increase the anode-film distance if so desired.

In the Caldwell position the other half of the 8 × 10 cassette is used and again immobility is attained by means of another horizontal bar which is placed somewhat higher and more posteriorly. The tube is angled about 10 to 12 degrees in this position (Fig. 4).

After both exposures have been made the exposed portion of the film is covered and the mask removed. A flash exposure is then made with the number and name in place. The result is a good view of the paranasal sinuses in both the Waters and Caldwell positions on one 8 × 10 inch cassette (Fig. 5).

For study of the mastoids both the horizontal bars are removed and the single upright piece is placed. With the head in the true lateral position, as judged by the radiologist or technician, it is held thus by asking the patient to bite onto the upright bar. It is readily seen that, with the jaws tightly clamped it is impossible for the head to be in other than a perfectly parallel plane with the cassette. Rotation of the head is also impossible after the jaws have been properly placed. The tube is then angled 15 degrees toward the feet and face

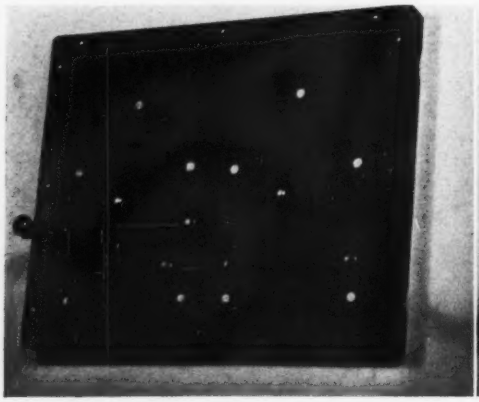

Fig. 1. Sinus board with cross bars in place for Waters and Caldwell positions.

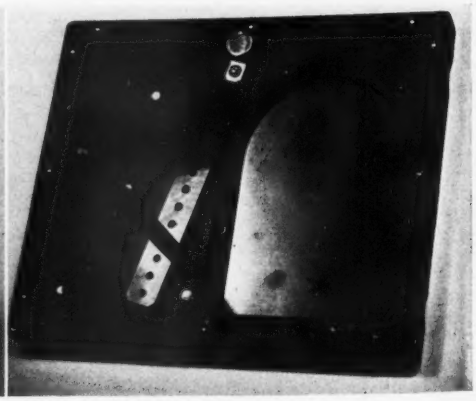

Fig. 2. Sinus "bite-mouths" removed and perpendicular bite-mouth in place for mastoids.

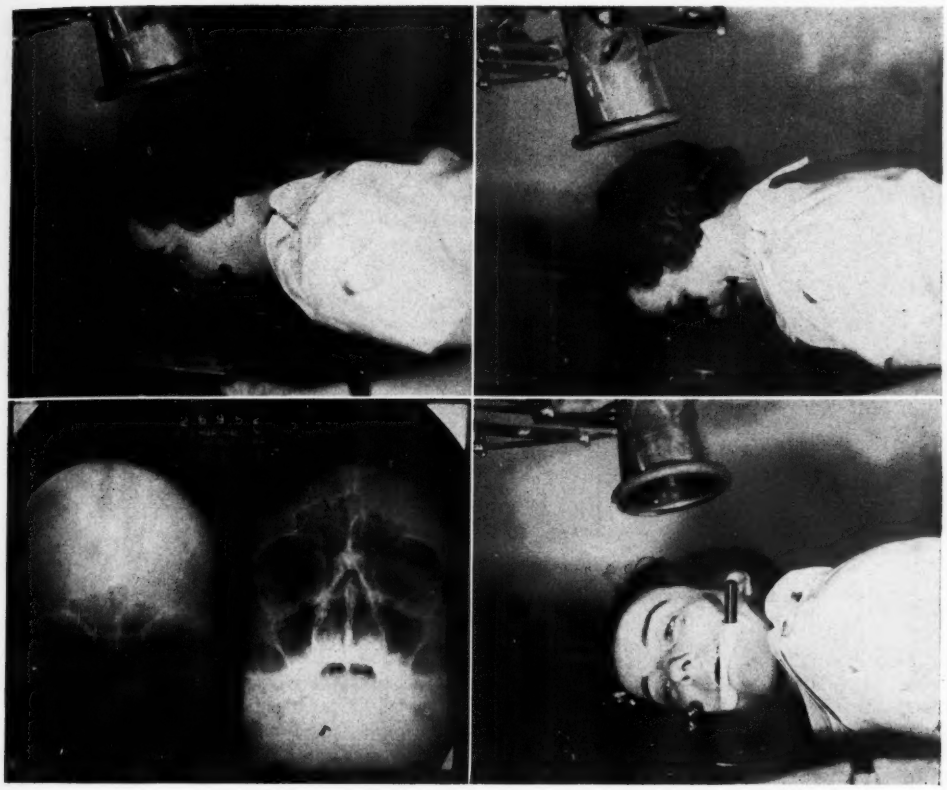

Fig. 3 (*upper left*). Method of holding head in Waters position by means of "bite-mouth." If desired, the nose may be elevated about 1.5 cm. above the cassette and the tube left perpendicular.

Fig. 4 (*upper right*). Method of maintaining head in Caldwell position by means of "bite-mouth." Tube is angled about 10 to 12 degrees, depending somewhat on the shape of the head.

Fig. 5 (*lower left*). Representative film made with "bite-mouth" type of sinus head rest.

Fig. 6 (*lower right*). Showing application of "bite-mouth" principle in maintaining head position for mastoids.

in the usual manner and the exposure made. As in the case of the sinuses, it is almost impossible for motion to occur during an exposure, providing, of course, the patient maintains his hold on the perpendicular bar. For this reason the length of exposure need not be taken into consideration and any desired combination of technical factors may be used (Fig. 6). The perpendicular bar is also used for lateral views of the frontal and sphenoid sinuses.

The same principle may be utilized for upright sinus films if attached to a suitable standard. A Lysholm grid may be used by simply inserting it between the cassette and the mask.

SUMMARY

In conclusion, a simple "bite-mouth" combination sinus-mastoid board has been described which greatly facilitates good position and immobility.

I wish to thank Mr. Walter Ferris, of the National Manufacturing Company, for his helpful suggestions and for the construction of the "board."

A NEW DEVICE FOR READING X-RAY FILMS[1]

By HENRY H. JORDAN, M.D., *New York City*

The constant improvement in the technic of roentgenography and the steady accumulation of case reports adding to our diagnostic experience ought to result in better x-ray interpretation. However, when more details are being reproduced by an x-ray film of higher sensitivity, a more intensive study of these

[1] U. S. Patent No. 2,079,373.

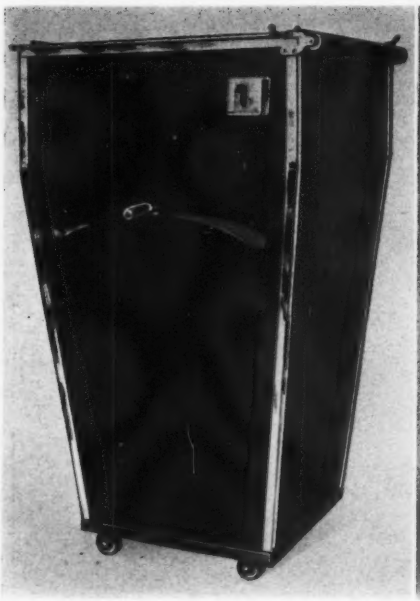

Fig. 1.

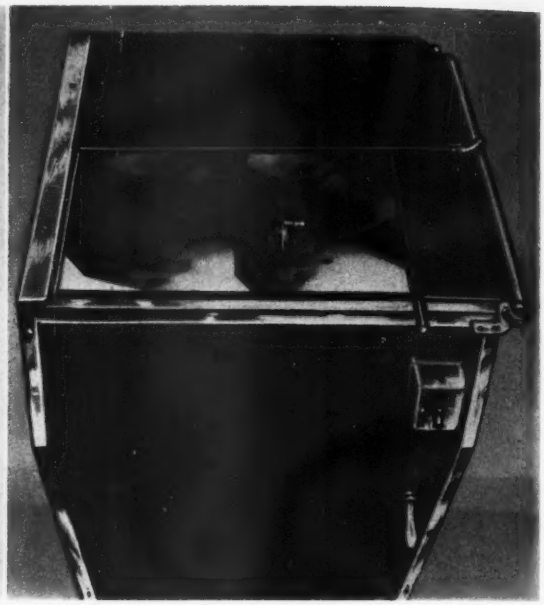

Fig. 2.

details becomes necessary, which demands an adaptation of the eye to the finer structure of the picture, in order to obtain an improved reading or interpretation of the film. In this respect, however, there seems to be much room for improvement, as the art of reading x-ray films is frequently not sufficiently supported by the technical devices used for their examination. And this is especially true when a case requires comparative study of various x-ray films taken at different times and under different conditions. In order to obtain maximum information from an x-ray film and to facilitate scientific interpretation, an x-ray illuminator of maximum efficiency is a prerequisite which ought to fulfill the following requirements:

1. Strongest possible source of light to illuminate even the darkest parts of an over-exposed film.

2. Finest regulation down to almost complete darkness in order to study the thin and under-exposed negatives.

3. Possibility to confine the field of view to any part of the film in order to obtain more contrast and to be able to concentrate on difficult structures.

4. The illuminator must be arranged for greatest possible convenience of the examining physician. He must be able to relax completely and concentrate on the study of details of the film without undue tiring.

5. It should be possible to make tracings of x-ray films (*e.g.*, spine cases) and to take measurements without having to fix the film with special gadgets.

6. Furthermore the viewing box should be handy; it should fit into small space; it should be movable in order to be used in the operating and plaster room as well as at the bedside, and finally it should be reasonably priced.

All these requirements are fulfilled by the viewing box (Figs. 1 and 2), which has been built based upon many years of experience.

One of the most important principles used in this new device is characterized by the fact that the entire apparatus is arranged vertically, thereby permitting a considerable saving in space without sacrificing the large distance from the source of the light to the film which is necessary to preserve the films from overheating in using strong sources of light.

Figure 3 shows a front view, a plane view, and a vertical section through the device.

The illuminator has the form of a vertical column of about the height of a table.

The casing (1) is made of sheet metal provided with an insulating lining (2) of asbestos. Four caster wheels (3) ensure easy moving. The film support at the upper end of the casing consists of a horizontal light-diffusing glass plate (5) preferably of bluish color. The field of view can be confined variably by two self-rolling curtains (17 and 18).

An electric bulb (9) of 1,500 watts is arranged in the center of the bottom (4) giving

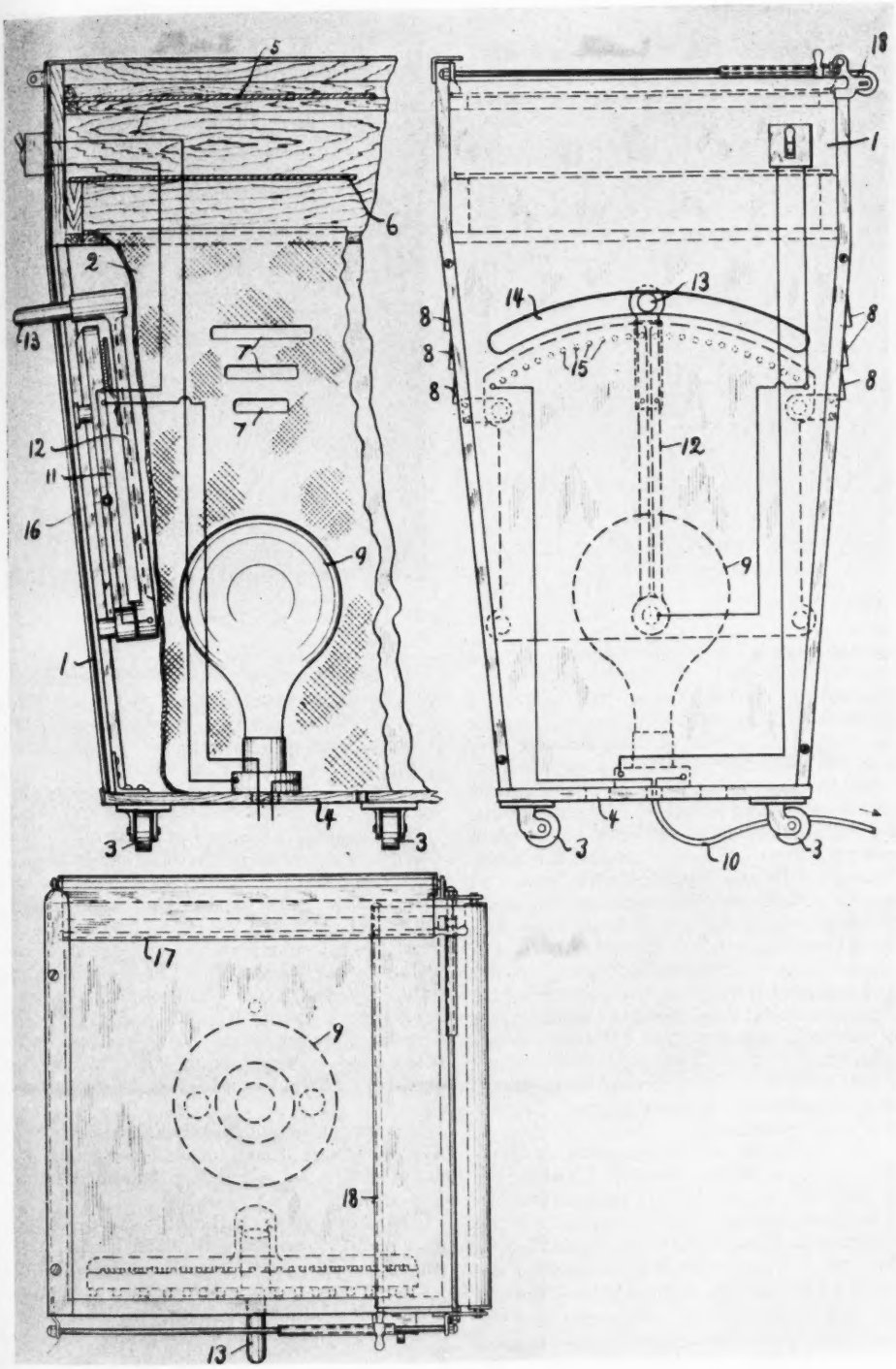

Fig. 3.

sufficient illumination for the study of even the darkest films.

A heavy rheostat (11) controlled by a crank (12), the handle (13) of which projects outwardly through an arcuate slot (14) permits finest regulation of light from almost complete darkness to full power of 1,500 watts.

The vertical arrangement of the apparatus provides sufficient distance between the strong source of light and the film and thereby prevents overheating of the film in spite of omission of special and complicated cooling devices.

The location of the heavy rheostat in the lower half of the viewing box serves as a weight for stabilizing the device.

The viewing box is about 90 cm. high; the base is 37 × 37 cm., and the top is 52 × 52 cm.

CONGENITAL CYSTIC DISEASE OF THE LUNG IN NEW-BORN INFANT[1]

By FRANCES A. FORD, M.D., *Detroit, Michigan*
Radiologist at Woman's Hospital

This report of a gradually expanding pulmonary cyst in a new-born infant diagnosed by roentgenologic examination and confirmed by autopsy findings, is presented to add to the increasing list of verified instances of congenital cystic disease of the lung.

The pathologic basis of pulmonary cystic disease has been ably described by Koontz, and by King and Harris in recent medical literature, but the condition is sufficiently rare so that even some pathologists of wide experience have expressed doubts of its occurrence as a truly congenital malformation.

Koontz believes that the cysts develop from occlusion of a portion of the bronchial tree during embryonic life, with subsequent expansion of the distal trunk by retained secretions. If the dilated terminal portion of the bronchus fails to rupture with establishment of respiration, a silent non-expansile structure remains. When communication between the cyst and the surrounding lung tissue does occur, various syndromes may develop, depending upon the freedom of ingress and egress of air.

A full term, male infant was born by spontaneous delivery on Nov. 29, 1936. The child's color was blue at birth, but the respirations were regular and the cry vigorous. Labored respirations and cyanosis were first noted 24 hours later. Oxygen therapy relieved these symptoms for 12 hours. After that time shallow,

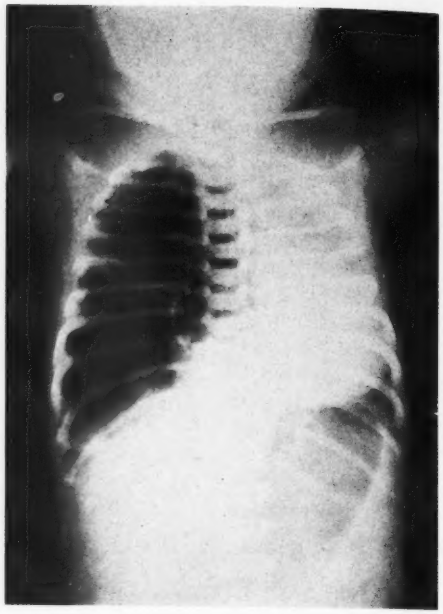

Fig. 1. Anteroposterior roentgenogram of the chest.

rapid breathing and dusky color recurred in attacks of increasing frequency and severity in spite of continuous oxygen therapy and medication for cardiac and respiratory stimulation. Excess mucus was noted in the patient's throat at times. A slight bulging of the anterior chest wall was detected on the third day and this increased gradually to the time of death.

A roentgenogram of the chest made 72 hours after birth showed atelectasis of the left lung with displacement of the heart and mediastinum to the left. In the right thorax the intercostal spaces were widened and the right diaphragm was depressed. The over-distended right lung was divided into a number of large, irregular air spaces by thin partitions of the density of fibrous bands. At the periphery and base of the lung were small areas of increased density. There was no evidence of pneumothorax.

A diagnosis of congenital cystic disease of the right lung and atelectasis of the left lung, with displacement of the heart and mediastinum was made.

The infant died on the fifth day (102 hours after birth). An autopsy made by Dr. D. C. Beaver, pathologist at Woman's Hospital, within a few hours after death revealed the following data:

The only pathology of significance was in the thoracic cavity. The diaphragm was at the seventh rib on the left in the midclavicular line,

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[1] This report is a preliminary contribution in a study of respiratory conditions in the newborn made possible by a grant from the Mendelsohn Fund, Detroit.

Fig. 2. The opened cyst ($3^1/_2 \times 2^1/_4 \times 1^1/_2$ inches).

Fig. 3. Photomicrograph of the cyst wall (×100).

and within 0.5 centimeter of the costal margin on the right. The pleural cavities contained no free fluid nor adhesions. The heart was displaced into the left thoracic cavity but showed no abnormality. The aorta and pulmonary trunk were normal. The left lung was of increased consistency and microscopic sections revealed moderate atelectasis. Most of the right upper and middle lobes presented a similar appearance, but in addition small areas of crepitant tissue, pink in color, occurred mainly at the periphery of the lobes. These portions showed moderate emphysema, microscopically. The lower lobe of the right lung was greatly enlarged, measuring 11 by 7 by 5.5 centimeters. It was light pink in color, translucent, and presented the appearance of a thin-walled cavity filled with air. The lower or diaphragmatic surface showed small areas of lung tissue varying from dark red to pink color, with only the margins exhibiting crepitation. The dilated sac-like portion of the lung when opened was found to be a single air-filled space, lined with smooth, glistening, fibrous tissue, arranged in strands which partially divided the cavity. Microscopically, the wall consisted of a surface layer of moderately high bronchial type epithelium supported on a definite but variable connective tissue membrane. The adjacent alveolar spaces opened into the cyst as they normally do into the bronchi. The lung tissue surrounding the cyst wall was normal, except for occasional large emphysematous spaces.

The trachea was normal, and a probe could be passed readily into the primary bronchus of the left lung, and into the upper and middle lobes on the right. A branch of the right lower bronchus, leading into the diaphragmatic portion of the lower lobe, was patent, but no macroscopic communication with the distended cyst could be found.

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KING, J. C., and HARRIS, L. C.: Congenital Lung Cyst. Jour. Am. Med. Assn., 1937, **108,** 274–280.

RADIUM BED

By S. S. MARCHBANKS, M.D., *Chattanooga, Tenn.*

The idea for the construction of this bed with a hinged footpiece (Fig. 1) was mothered by necessity.

I administer radium to quite a number of cases of cancer of the uterine cervix in my office, having rooms for this purpose.

On two occasions, when lifting the patient back from the foot of the bed, even with the

assistance of the nurse, I have strained my back severely, so the type of bed illustrated was invented.

foot rests for an ordinary pelvic examination, although, of course, stirrups are used when radium is administered.

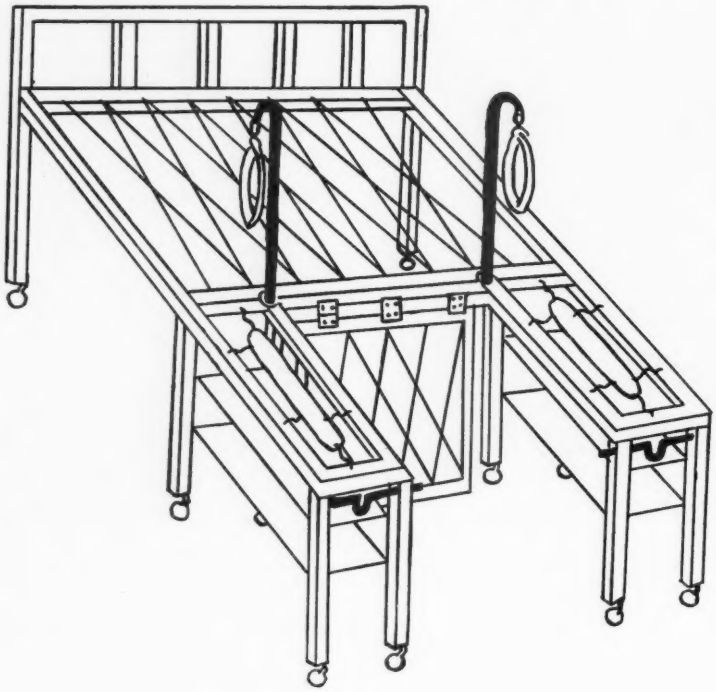

Fig. 1.

We had a local manufacturer of beds make this one. The footpiece is held up by two slide pins. The mattress is so divided that it folds down easily at the foot, leaving two lateral sections which are quite satisfactory for

This type of bed is also useful when, as in office buildings, conservation of space is necessary. When the footpiece is down, one has ample room for all necessary operative movements.

GENERALIZED OSSIFYING PERIOSTITIS[1]

REPORT OF A CASE

By J. N. ODESSKY, M.D., *and* P. A. SHIRSHNEV, M.D., *Moscow, U. S. of S. R.*

Patient S., male, 51 years of age, was admitted to the clinic on Dec. 24, 1936 (History N 5855), complaining of dyspnea, palpitation of the heart on the slightest physical exertion, constant pain in the region of the heart, a cough with expectoration, and pain in the lower limbs.

[1] From the Radiological Service of the Ostroumoff Clinical Hospital, named after Prof. A. Zeitlin, from the Department of Roentgenology (Director, Prof. A. Zeitlin, M.D.), and from the Propedeutic Clinic (Director, Prof. L. Fogelson, M.D.), of the Third Moscow State Medical Institute.

Two months earlier his illness began with a gradually increasing dyspnea and weakness. In February, 1936, he had fractured both bones of the right leg as the result of a fall. In October he noted the appearance of edema, first on one ankle than on the other and on the wrists.

Physical Examination.—The patient was of middle height, of less than normal build, active. His skin was dry, with no eruptions. The movement of the joints was somewhat limited. The distal ends of the bones of the forearms and the lower limbs (Figs. 1, 2, and 3) were markedly thickened; the finger tips were somewhat clubbed.

Percussion of the lungs revealed a hyperresonance on both sides, with the exception of the region under the lower angle of the scapula,

where a diminution of resonance was noted. Auscultation showed a great number of dry sibilant sounds and a number of râles in the

Fig. 1.

region where percussion sound was dulled. The sputum was of muco-purulent character but without admixture of blood.

The Heart.—The dullness extended to the left 1 cm. beyond the linea medio-clavicularis and to the right 1 cm. beyond the right sternal border. The tones of the heart were dull; no murmurs were heard. The blood pressure was 140/80.

Examination of the gastro-intestinal tract, kidneys, and nervous system showed no abnormalities.

Analysis of Urine.—Color, yellowish; reaction, acid; specific gravity, 1.015. Under the microscope, a small number of leukocytes, epithelium, and mucus.

The blood count showed hemoglobin, 59 per cent; erythrocytes, 3,690,000; color index, 0.8; leukocytes, 11,600; neutrophiles, 69 per cent; stablike, 8.5 per cent; lymphocytes, 17 per cent, and monocytes, 5 per cent. The erythrocyte sedimentation test was 35 mm. per hour (Panshenkoff apparatus). Examination of the sputum showed a few erythrocytes, quite a great

Fig. 2.

Fig 3.

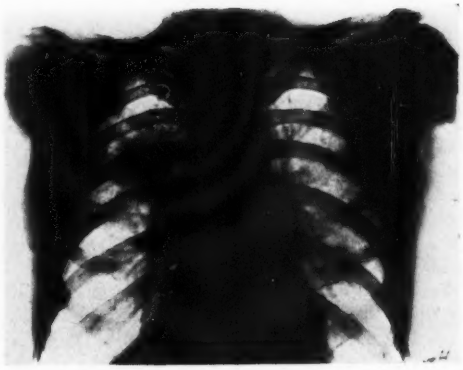

Fig. 4.

Fig. 5.

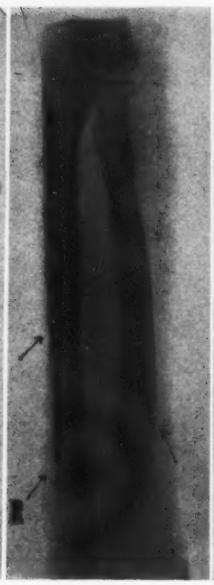

Fig. 6.

Fig. 7.

quantity of spirochetes, a few streptococci and Pfeiffer bacilli. No Koch bacilli or elastic fibers were found (after repeated examination). The Wassermann reaction was negative.

ROENTGENOGRAM OF THE CHEST

Dec. 29, 1936: The right upper lobe of the lungs was diffusely clouded; a more distinct shadow was apparent at the level of the third intercostal space. The rest of the lung was clear. The right hilus was more massive than the left. The broncho-vascular shadow was somewhat accentuated. The sinuses were free. The mobility of both diaphragmal cupola was slight.

The roentgenologic examination of the heart revealed a slightly dilated left ventricle; the vascular shadow was somewhat lengthened and was wider than normal.

Jan. 15, 1937: The right upper lobe was clouded. A more compact shadow was seen between the second and third intercostal spaces; its character was not, however, quite homogeneous but there were intermittent clearer shadows. In the lower medial part these shadows touched the upper end of the right sinus.

Feb. 7, 1937: The diffuse heavy shadow of the upper lobe disappeared, leaving a clear picture of the lung, with the exception of the compact shadow in the central part, which remained unchanged.

March 7, 1937: The compact area in the lung on the level of the second and third intercostal spaces remained unchanged, but its character became more homogeneous (Fig. 4).

March 28, 1937: No changes from above noted in the roentgenograph.

ROENTGENOGRAMS OF THE UPPER LIMBS (FIGS. 5, 6)

On the diaphysis of both humeri was seen a periosteal deposit, more slight on the anterior and more compact on the posterior surface. In the proximal parts of both bones of the forearm no changes were noted. The rest of the bones, along their entire length, were enveloped by periosteal deposits. Their contours were smooth in some places and serrated in others. In the metaphysis of the distal end of the radius, the periosteal growths were divided from the medullar layer by a lighter stratum. Beginning from the middle of the lateral part of the ulnar bone the periosteal layer widened toward the distal end, reaching 3 mm. in width. Also the diaphyses of the carpal bones, the basic and second phalanges were enveloped by periosteal deposits which were more accentuated on the first and fifth carpal, and second, third, and fourth basal phalanges.

The nail phalanges were unchanged. The joints were normal; the articular fissures were of normal width.

Fig. 8.

Fig. 9.

Fig. 10.

ROENTGENOGRAMS OF THE LOWER LIMBS
(FIGS. 7, 8, 9, 10)

Along the entire length of the femoral bones were noted periosteal growths. In the proximal end of the right femur, beginning from the trochanter major and reaching to the middle third of the bone, the periosteal deposit reached from 2 to 5 mm. in width, and from the trochanter minor toward the lower third its width was equal to from 1 to 2 mm. On a limited area of about 4 cm. on the margin of the middle and lower third of the femur the width of the periosteal layer reached even 6 mm. The medullar layer was quite distinctly seen. The hip and knee joints revealed no changes. The articular fissure was normal. On the left leg the periosteal layer on the exterior surface along the entire length of the fibula reached from 1 to 2 mm. in width; on the interior surface it was noted only on the lower half of the bone. The contours were serrated. The upper two-thirds of the lateral surface of the tibia and the lower two-thirds of its medial surface had periosteal deposits from 2 to 5 mm. wide. They presented a jagged appearance on the exterior surface and were smooth on the interior surface.

The right leg showed an old fracture of the upper third of the fibula and lower third of the tibia. There were also noted considerable periosteal growths along both bones with the exception of the inferior surface of the metaphyseal part of the proximal end of the tibia. The entire surface of the periosteal deposit was serrated. Its width reached about 6 mm.

The bones of the feet showed periosteal growths clearly expressed along the diaphyses of all the bones of the metatarsus and basal phalanges; the jagged character of the contours was accentuated. The nail phalanges remained unchanged. The ankle joints were normal; the articular fissures were of normal width. The bones presented a porous appearance.

DIAGNOSIS

Pierre-Marie-Bamberger's disease (generalized ossifying periostitis); right-sided catarrhal pneumonia; cardiosclerosis.

DISCUSSION

Cases of generalized ossifying periostitis of the long bones are quite rare. In the world literature there appeared descriptions of about 175 cases during the period of fifty years, of which only about 30 cases have had histologic investigations.

However, there is no unity on the concept of pathogenesis of the disease. Most authors agree that ossifying periostitis is a secondary disease and not a disease *sui generis*, since it might appear in the course of various chest affections, such as tuberculosis, pneumonia, empyema, abscesses, bronchiectasis, malignant tumors (original and of metastatic origin), blastomycosis, cardiac diseases, etc. This leads one to the belief that the development of an ossifying periostitis may depend upon pathologic changes in the lungs. However, the question whether all the above-mentioned diseases of the lungs may really be held responsible for the appearance of this disease is still open. Patients suffering from one or another

of the above affections of the lungs are numerous but only few develop Pierre-Marie-Bamberger's disease. In more than twenty cases ossifying periostitis could not be regarded as a secondary manifestation since there was no preliminary disease to which it could be ascribed. Thus the etiologic factor remained in these cases unknown. The question was clarified neither by the work of Bamberger nor by the more recent reports of the American authors, Compere, Adams, and Compere. These authors could not produce the process experimentally and came to the conclusion that the causative factor of this disease is yet unknown.

The symptoms presented by our patient could be summarized as follows: characteristic for the Marie-Bamberger's disease was the symmetrical enlarging of the upper and lower extremities with expressed clubbing of the finger tips. Roentgenologically there were revealed periosteal deposits along the entire length of the long bones, also on the carpal, tarsal, and basal phalanges, with the exception of the nail phalanges. According to the literature these symptoms develop chronically and the patient cannot tell when the first signs of the disease appeared. However, there are cases in which the development of the symptoms proceeds rapidly and their onset can be revealed quite distinctly. To this latter group evidently belongs our patient. As noted above, three or four months previous to admittance into the clinic he noted an edema of the ankles and wrists. In our case were found definite pathologic changes in the lungs, but it would be incorrect to ascribe the development of the ossifying process to this lesion of the lungs since it might be an accidentally concurrent process.

RADIOLOGICAL SOCIETIES IN THE UNITED STATES

CALENDAR

Editor's Note.—Will secretaries of societies please cooperate with the Editor by supplying him with information for this section.

CALIFORNIA

California Medical Association, Section on Radiology.—Chairman, John D. Lawson, M.D., 1306 California State Bldg., Sacramento; *Secretary,* Karl M. Bonoff, M.D., 1930 Wilshire Blvd., Los Angeles. Meets annually with California Medical Association.

Los Angeles County Medical Association, Radiological Section.—President, John F. Chapman, M.D., 65 N. Madison Ave., Pasadena; *Vice-president,* E. N. Liljedahl, M.D., 1241 Shatto St.; *Secretary,* Merl L. Pindell, M.D., 678 South Ferris Ave.; *Treasurer,* Henry Snure, M.D., 1414 Hope Street. Meets every second Wednesday of month at County Society Building.

Pacific Roentgen Club.—Chairman, Raymond G. Taylor, M.D., 1212 Shatto St., Los Angeles; *Secretary,* L. Henry Garland, M.D., 450 Sutter St., San Francisco.

San Francisco Radiological Society.—Secretary, L. H. Garland, M.D., 450 Sutter Street. Meets monthly on first Monday at 7:45 P.M., alternately at Toland Hall and Lane Hall.

COLORADO

Denver Radiological Club.—President, John S. Bouslog, M.D., 246 Metropolitan Bldg.; *Vice-president,* Sanford Withers, M.D., 304 Republic Bldg.; *Secretary,* Ernst A. Schmidt, M.D., Colorado General Hospital; *Treasurer,* H. P. Brandenburg, M.D., 155 Metropolitan Bldg. Meets third Tuesday of each month at homes of members.

CONNECTICUT

Connecticut State Medical Society, Section on Radiology.—Chairman, Kenneth K. Kinney, M.D., 29 North Street, Willimantic; *Vice-chairman,* Francis M. Dunn, M.D., 100 State Street, New London; *Secretary-Treasurer,* Max Climan, M.D., 242 Trumbull St., Hartford. Meetings twice annually in May and September.

DELAWARE

Affiliated with Philadelphia Roentgen Ray Society.

FLORIDA

Florida State Radiological Society.—President, Gerald Raap, M.D., 168 S. E. First St., Miami; *Vice-president,* H. O. Brown, M.D., 404 First Nat'l Bank Bldg., Tampa; *Secretary-Treasurer,* H. B. McEuen, M.D., 126 W. Adams St., Jacksonville.

GEORGIA

Georgia Radiological Society.—President, James J. Clark, M.D., Doctors Bldg., Atlanta; *Vice-president,* William F. Lake, M. D., Medical Arts Bldg., Atlanta; *Secretary-Treasurer,* Robert C. Pendergrass, M.D., Prather Clinic, Americus. Meetings twice annually, in November and at the annual meeting of the Medical Association of Georgia in the spring.

ILLINOIS

Chicago Roentgen Society.—President, David S. Beilin, M.D., 411 Garfield Ave.; *Vice-president,* Chester J. Challenger, M.D., 3117 Logan Blvd.; *Secretary-Treasurer,* Roe J. Maier, M.D., 7752 Halsted St. Meets second Thursday of each month, September to May, except December.

Illinois Radiological Society.—President, Ivan Brouse, M.D., 316 W. State, Jacksonville; *Vice-president,* Cesar Gianturco, M.D., Carle Hospital Clinic, Urbana; *Secretary-Treasurer,* Edmund P. Halley, M.D., 968 Citizens Bldg., Decatur. Meetings quarterly by announcement.

Illinois State Medical Society, Section of Radiology.—President, Roswell T. Pettit, M.D., 728 Columbus St., Ottawa; *Secretary,* Ralph G. Willy, M.D., 1138 N. Leavitt St., Chicago.

INDIANA

Indiana Roentgen Society.—President, J. N. Collins, M.D., 23 E. Ohio St., Indianapolis; *President-elect,* Stanley Clark, M.D., 108 N. Main St., South Bend; *Vice-president,* Juan Rodriguez, M.D., 2903 Fairfield Ave., Fort Wayne; *Secretary-Treasurer,* Clifford C. Taylor, M.D., 23 E. Ohio St., Indianapolis. Annual meeting in May.

IOWA

The Iowa X-ray Club.—Holds luncheon and business meeting during annual session of Iowa State Medical Society.

MAINE

See New England Roentgen Ray Society.

MARYLAND

Baltimore City Medical Society, Radiological Section.—Chairman, Marcus Ostro, M.D., 1810 Eutaw Place; *Secretary,* H. E. Wright, M.D., 101 W. Read St., Baltimore. Meetings second Tuesday of each month.

MASSACHUSETTS

See New England Roentgen Ray Society.

MICHIGAN

Detroit X-ray and Radium Society.—President, E. W. Hall, M.D., 10 Peterboro Street; *Vice-president,*

Sam W. Donaldson, M.D., 326 North Ingalls St., Ann Arbor; *Secretary-Treasurer*, E. R. Witwer, M.D., Harper Hospital. Meetings first Thursday of each month from October to May, inclusive, at Wayne County Medical Society Bldg.

Michigan Association of Roentgenologists.—President, E. R. Witwer, M.D., Harper Hospital, Detroit; *Vice-president*, D. W. Patterson, M.D., 622 Huron Street, Port Huron; *Secretary-Treasurer*, C. K. Hasley, M.D., 1429 David Whitney Bldg., Detroit.

MINNESOTA

Minnesota Radiological Society.—President, Walter H. Ude, M.D., 78 S. 9th St., Minneapolis; *Vice-president*, Leo G. Rigler, M.D., University Hospitals, Minneapolis; *Secretary-Treasurer*, Harry Weber, M.D., 102 Second Ave., S. W., Rochester. Meetings quarterly.

MISSOURI

The Kansas City Radiological Society.—President, L. G. Allen, M.D., 907 N. 7th St., Kansas City, Mo.; *Secretary*, Ira H. Lockwood, M.D., 306 E. 12th St., Kansas City, Mo. Meetings last Thursday of each month.

The St. Louis Society of Radiologists.—President, Joseph C. Peden, M.D., 634 N. Grand Blvd.; *Secretary*, W. K. Mueller, M.D., 607 N. Grand Blvd. Meetings fourth Wednesday of each month.

NEBRASKA

Nebraska Radiological Society.—President, E. W. Rowe, M.D., 128 N. 13th St., Lincoln; *Secretary*, D. Arnold Dowell, M.D., 117 S. 17th St., Omaha. Meetings first Wednesday of each month at 6 P.M. in Omaha or Lincoln.

NEW ENGLAND ROENTGEN RAY SOCIETY

(Maine, New Hampshire, Vermont, Massachusetts, and Rhode Island.) *President*, Frank E. Wheatley, M.D., 520 Beacon St., Boston; *Secretary*, E. C. Vogt, M.D., 300 Longwood Ave., Boston. Meetings third Friday of each month from October to May, inclusive, usually at Boston Medical Library.

NEW HAMPSHIRE

See New England Roentgen Ray Society.

NEW JERSEY

Radiological Society of New Jersey.—President, J. D. Tidaback, M.D., 382 Springfield, Summit; *Vice-president*, Milton Friedman, M.D., Newark Beth Israel Hospital, Newark; *Secretary*, P. S. Avery, M.D., 546 Central Ave., Bound Brook. Meetings at Atlantic City at time of State Medical Society, and Midwinter in Newark as called by president.

NEW YORK

Brooklyn Roentgen Society.—President, Albert Voltz, M.D., 115–120 Myrtle Avenue, Richmond Hill; *Vice-president*, A. L. L. Bell, M.D., Long Island College Hospital, Henry, Pacific, and Amity Sts., Brooklyn; *Secretary-Treasurer*, E. Mendelson, M.D., 132 Parkside Ave., Brooklyn. Meetings first Tuesday in each month at place designated by president.

Buffalo Radiological Society.—President, John Barnes, M.D., 875 Lafayette Ave.; *Vice-president*, W. L. Mattick, M.D., 290 Highland Drive; *Secretary-Treasurer*, J. S. Gian-Franceschi, M.D., 610 Niagara Street. Meetings second Monday evening each month.

Central New York Roentgen-ray Society.—President, W. E. Achilles, M.D., 60 Seneca St., Geneva; *Vice-president*, M. T. Powers, M.D., 250 Genesee St., Utica; *Secretary-Treasurer*, Carlton F. Potter, M.D., 425 Waverly Ave., Syracuse. Meetings held in January, May, and October as called by Executive Committee.

Long Island Radiological Society.—President, David E. Ehrlich, M.D., 27 W. 86th St., New York City; *Vice-president*, H. Koiransky, M.D., 43–37 47th St., Long Island City; *Secretary*, S. Schenck, M.D., 115 Eastern Parkway, Brooklyn; *Treasurer*, Moses Goodman, M.D., 45–01 Skillman Ave., Long Island City. Meetings third Thursday evening each month at Kings County Medical Bldg.

New York Roentgen Society.—President, E. F. Merrill, M.D., 30 W. 59th St., New York City; *Vice-president*, I. W. Lewis, M.D.; *Secretary*, H. K. Taylor, M.D., 667 Madison Ave., New York City; *Treasurer*, R. D. Duckworth, M.D., 170 Maple Ave., White Plains. Meetings third Monday evening each month at Academy of Medicine.

Rochester Roentgen-ray Society.—Chairman, Joseph H. Green, M.D., 277 Alexander St.; *Secretary*, S. C. Davidson, M.D., 277 Alexander St. Meetings at convenience of committee.

Society of Radiological Economics of New York.—President, Albert L. Voltz, M.D., 115–120 Myrtle Ave., Richmond Hill; *Vice-president*, M. M. Pomeranz, M.D., 911 Park Ave., New York City; *Secretary*, W. F. Francis, M.D.; *Treasurer*, Theodore West, M.D., United Hospital, Port Chester. Meetings first Monday evening each month at McAlpin Hotel.

NORTH CAROLINA

Radiological Society of North Carolina.—President, Robert P. Noble, M.D., 127 W. Hargett St., Raleigh; *Vice-president*, A. L. Daughtridge, M.D., 144 Coast Line St., Rocky Mount; *Secretary-Treasurer*, Major I. Fleming, M.D., 404 Falls Road, Rocky Mount. Meetings with State meeting in May, and meeting in October.

OHIO

Cleveland Radiological Society.—President, North W. Shetter, M.D., Lakewood City Hospital, Lakewood; *Vice-president*, John Heberding, M.D., St. Eliza-

beth's Hospital, Youngstown; *Secretary-Treasurer*, Harry Hauser, M.D., Cleveland City Hospital, Cleveland. Meetings at 6:30 P.M. at Cleveland Chamber of Commerce Club on fourth Monday of each month from October to April, inclusive.

Radiological Society of the Academy of Medicine (Cincinnati Roentgenologists).—*President*, George Benzing, M.D., St. Elizabeth Hospital, Covington, Ky.; *Secretary-Treasurer*, Justin E. McCarthy, M.D., 707 Race St., Cincinnati, Ohio. Meetings held third Tuesday of each month.

PENNSYLVANIA

Pennsylvania Radiological Society.—President, Sydney J. Hawley, M.D., Geisinger Memorial Hospital, Danville; *First Vice-president*, William J. McGregor, M.D., 744 Franklin Ave., Wilkinsburg; *Second Vice-president*, Oscar M. Weaver, M.D., 12 S. Main St., Lewistown; *Secretary-Treasurer*, Lloyd E. Wurster, M.D., 416 Pine St., Williamsport; *President-elect*, Charles S. Caldwell, M.D., 520 S. Aiken Ave., Pittsburgh. Annual meeting, May, 1938. Exact date and place to be decided.

Philadelphia Roentgen Ray Society.—President, Thomas P. Laughery, M.D., Germantown Hospital; *Vice-president*, Elwood E. Downs, M.D., Jeans Hospital, Fox Chase; *Secretary*, Barton H. Young, M.D., Temple University Hospital; *Treasurer*, R. Manges Smith, M.D., Jefferson Hospital. Meetings first Thursday of each month from October to May, Thompson Hall, College of Physicians, 19 S. 22nd St., 8:15 P.M.

The Pittsburgh Roentgen Society.—President, F. L. Schumacher, M.D., Jenkins Arcade; *Secretary*, H. N. Mawhinney, M.D., Mercy Hospital. Two Fall and two Spring meetings at time and place designated by president.

RHODE ISLAND

See New England Roentgen Ray Society.

SOUTH CAROLINA

South Carolina X-ray Society.—President, Robert B. Taft, M.D., 105 Rutledge Ave., Charleston; *Secretary-Treasurer*, Hillyer Rudisill, M.D., Roper Hospital, Charleston. Meetings in Charleston on first Thursday in November, also at time and place of South Carolina State Medical Association.

SOUTH DAKOTA

Meets with Minnesota Radiological Society.

TENNESSEE

Memphis Roentgen Club.—Chairmanship rotates monthly in alphabetical order. Meetings second Tuesday of each month at University Center.

Tennessee State Radiological Society.—President, H. S. Shoulders, M.D., 246 Doctors Bldg., Nashville; *Vice-president*, S. S. Marchbanks, M.D., 508 Medical Arts Bldg., Chattanooga; *Secretary-Treasurer*, Franklin B. Bogart, M.D., 311 Medical Arts Bldg., Chattanooga. Meeting annually with State Medical Society in April.

VERMONT

See New England Roentgen Ray Society.

VIRGINIA

Radiological Society of Virginia.—President, Fred M. Hodges, M.D., 100 W. Franklin St., Richmond; *Vice-president*, L. F. Magruder, M.D., Raleigh and College Aves., Norfolk; *Secretary*, V. W. Archer, M.D., University of Virginia Hospital, Charlottesville.

WASHINGTON

Washington State Radiological Society.—President, H. E. Nichols, M.D., Stimson Bldg., Seattle; *Secretary*, T. T. Dawson, M.D., Fourth and Pike Bldg., Seattle. Meetings fourth Monday of each month at College Club.

WISCONSIN

Milwaukee Roentgen Ray Society.—Secretary, S. A. Morton, M.D., Columbia Hospital, Milwaukee. Meets monthly on first Friday.

Radiological Section of the Wisconsin State Medical Society.—Secretary, Russel F. Wilson, M.D., Beloit Municipal Hospital, Beloit. Two-day annual meeting in May and one day in connection with annual meeting of State Medical Society, in September.

University of Wisconsin Radiological Conference.—Secretary, E. A. Pohle, M.D., 1300 University Ave., Madison, Wis. Meets every Thursday from 4 to 5 P.M., Room 301, Service Memorial Institute.

NEWS ITEM

Conference of Eastern Radiologists (Philadelphia Session), sponsored by Philadelphia Roentgen Ray Society, met Jan. 28, 29, 1938. Program of 41 papers. Experiment was tried of holding all sessions in one central meeting place, and a ballot was to be taken to determine the success or failure of plan.

EDITORIAL

LEON J. MENVILLE, M.D., *Editor* HOWARD P. DOUB, M.D., *Associate Editor*

EARLY DIAGNOSIS OF BREAST CARCINOMA

It is the experience of physicians that too large a number of breast cancer cases are advanced when treated. There are many reasons for this, but the most important one is that a diagnosis is not made in the early stages of the disease. We so often hear physicians admonish women to be on their guard for cancer of the breast, and if they observe a lump in the breast, to go immediately to their physician. When a lump in the breast is discovered, if it is cancer, it is usually no longer considered an early case.

From one of our largest medical centers are reported certain statistics to the effect that from 35 to 50 per cent of cancers of the breast are inoperable when first seen, and 62 per cent of cancers of the breast have already metastasized when first seen.

For this reason, efforts have been made to diagnose carcinoma of the breast in its earliest stage, even in its pre-cancerous stage. Pre-cancerous conditions such as papillomas, Paget's disease of the nipple, and Schimmelbusch's disease, if diagnosed early and properly treated, may be the means of saving many cases from developing cancer, and in this manner the mortality rate will be appreciably diminished.

In appreciation of their importance, many different methods of examination have been employed, all of which have been found of value, either singly or in combination. For a long time dependence for the diagnosis of such cases has been placed upon transillumination. By this means it is possible, at times, when employed by competent hands, to differentiate between cysts containing clear fluid and solid tumors. It is helpful in the diagnosis of hematoma of the breast following trauma, and also in helping to localize duct papillomas. However, it has its limitations; for instance, it is not of much value in differentiating between benign and malignant solid tumors such as fibro-adenoma and carcinoma. While this type of examination in the hands of the experienced physician is of importance, frequently in diagnosing pre-cancerous and early cancer of the

HOWARD P. DOUB, M.D.

It has become a pleasant custom for readers to find, each year, in RADIOLOGY, *a portrait of the President of the Radiological Society of North America. This year especial significance is added by the fact that the President is also the Associate Editor of the Journal.*

Howard P. Doub was born in Hagerstown, Maryland, in 1890. He took his A.B. degree at Western Maryland College, later graduating in medicine from Johns Hopkins University, Baltimore. He is Radiologist at the splendid Henry Ford Hospital, in Detroit. He is a member of the American Roentgen Ray Society, the American Radium Society, the College of Radiology, a Fellow of the American Medical Association, and a diplomate of the American Board of Radiology, among other medical society affiliations.

Since the Society founded its present Journal, RADIOLOGY, *Dr. Doub has been a contributor to, and through the years he has evidenced deep interest in its progress. He has a marked faculty for calmly judging all phases of a question before he speaks concerning it.*

Dr. Doub has held office in the Society as Chairman of the Executive and Publication committees and as member of various other committees, so that he was intimately acquainted with its development and business affairs when he was chosen for its presidency. He is thoroughly respected as a scientist, well liked as an individual, and the Society has honored itself in the choice of Howard P. Doub for President.

Portrait by Lee F. Redman, Detroit

HOWARD P. DOUB, M.D.

PRESIDENT OF THE RADIOLOGICAL SOCIETY OF NORTH AMERICA

breast, it has, however, very definite limitations.

The question of biopsy in mammary cancer is so well known that it probably needs no comment here, except to say that some of our leading pathologists agree that even this method at times proves difficult. As eminent a pathologist as Dr. James Ewing (1) is reported in the "Bulletin of the American Society for the Control of Cancer" as stating:

> "There are some lesions in the breast in which it is difficult for any surgeon or pathologist to state positively whether the condition is malignant or benign. Hence, the surgeon must not assume that by obtaining a microscopic diagnosis he has secured positive information. In such cases the clinical data, age of patient, extent and duration of the disease, condition of lymph nodes, and especially the gross character of the lesion should be given much importance in the decision. Under these circumstances, some surgeons would err on the side of caution and perform the radical operation. I believe it is unfair to the patient to perform a radical mastectomy unless the diagnosis of carcinoma is positive. There are many precancerous and suspicious lesions in the breast which are clinically benign, while a true carcinoma is nearly always obvious to a pathologist of adequate experience. When a substantial doubt exists about the nature of a microscopic section of a breast tumor, it is generally not cancer."

Roentgenographic examination of the breast, popularized by Lockwood (2) and others, has also proven of value and has been the means of demonstrating many conditions affecting the breast such as mazoplasia, cystiphorous desquamative epithelial hyperplasia, fibro-adenoma, chronic cystic mastitis, fibrosis of the breast, lymph nodes in the axilla, carcinoma, etc.

Recently Hicken (3) reported certain observations made by a new method of examining the breast obtained by injecting thorium dioxide (thorotrast) into the ducts of the gland, followed by roentgen examination. This method of diagnosis is termed mammography. In this manner the ducts and their ramifications are clearly outlined. A careful study of the normal virginal breast and the multiparous breast was made and studied in order that the abnormal might be better understood. This method of examination, which is of very recent date, has clearly outlined in certain instances such conditions as papilloma, lipoma, cyst, and carcinoma. The technic is clearly and fully outlined in recent contributions (2 and 3).

There has been a considerable discussion in regard to the danger of the use of thorium dioxide as a diagnostic means in medicine on account of its radio-active principle. This has been in instances wherein it has been injected intravenously when it is readily taken up by the reticulo-endothelial system where it remains for a very long period of time. It would seem that the use of thorium dioxide as it is employed in mammography would not be considered dangerous.

In mammography we apparently have a method of examining the breast which will lead, along with the methods already mentioned, to an early diagnosis of disease conditions.

We all appreciate that rapid advancement is being made in the diagnosis of the pre-cancerous state and of early cancer of the breast, which indicates the great interest constantly being manifested in regard to the control of cancer of this organ.

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(2) Lockwood, Ira H., and Stewart, Wendell: Roentgen Study of Physiologic and Pathologic Changes in Mammary Gland. Jour. Am. Med. Assn., Oct. 29, 1932, **99,** 1461.

(3) Hicken, N. F.: Mammography: The Roentgenographic Diagnosis of Breast Tumors by Means of Contrast Media. Surg., Gynec. and Obst., March, 1937, **64,** 593.

ANNOUNCEMENT

AMERICAN PHYSICIANS' ART ASSOCIATION

The American Physicians' Art Association, a national organization of medical men who have ability in the fine arts, will hold a *first national exhibition* in the San Francisco Museum of Art, San Francisco, in June, 1938. (The American Medical Association Session will be held June 13–17 in the same city.) The American Physicians' Art Association already has an outstanding membership. There are three classifications for membership: active, associate,

and contributing. The *first annual exhibition* promises to be of unusual interest with entries to be accepted (after jury selection) in the following classifications: oils, water colors, sculpture, photography, pastels, etchings, crayon and pen and ink drawings (including cartoons), wood carvings, and book bindings. Scientific medical art work will not be accepted. The exhibition is not limited to first showings. All entries close April 1, 1938. Any physician interested should communicate at once with the Secretary of the American Physicians' Art Association, Suite 521–536 Flood Bldg., San Francisco, California.

IN MEMORIAM

FRANCIS P. GARVAN

An expression of regret and sympathy over the passing of Francis P. Garvan on November 7, 1937, seems tardy at this date, but the sad fact has only now come to the knowledge of some of us who knew Mr. Garvan as a generous benefactor of chemistry and of the study of disease and not at all as an individual. "The American Journal of Cancer," in its December, 1937, issue, contains a splendid editorial concerning Mr. Garvan's career. That Journal was the recipient of a generous share of his beneficence, as was also RADIOLOGY and individual research workers: Mr. Garvan gave freely of the funds at his command for the furtherance of medicine and chemistry.

In a biographical sketch, "Chemical Industries" says: "Being a man of vibrant energy and brilliant ability, he was able to accomplish many important, tangible things for those educational and industrial causes to which he devoted himself. Such service as he gave will be sorely missed; but to the hundreds of chemical people who had felt the firm grip of his hand, who knew the twinkle in his blue eyes, who had come to appreciate the jut of his jaw and the pound of his fist when he was thoroughly aroused, his passing means a more intangible but quite irreparable loss. It was his confidence in the American people, his loyalty to his friends; it was the courage with which he backed his convictions and the doggedness with which he followed his ideals; it was his bright optimism, his Celtic wit, his warm sincerity—these are the gifts he bestowed freely which cannot be replaced."

"The Wall Street Journal," in a lengthy comment on Mr. Garvan's career, said: "His interest in the American chemical industry dated from the War when, as Alien Property Custodian, he took over the seized German chemical patents. These patents, covering many important German processes for manufacturing dyes and pharmaceuticals, were bought from the Government by the Chemical Foundation and leased to American manufacturers on a royalty basis.

"The funds received from this source were used in research, for scholarships, and to promote an American chemical industry. Mr. Garvan was one of the most dynamic and dramatic of characters, with a mind always working along untrodden lines.

"Many of his ideas, at variance with the general thought of the time when he evolved them, since have become a widely accepted part of our national thought. He was an ardent nationalist and worked untiringly to promote his belief that America must be industrially and financially self-contained and free from dependence on European scientists or capital.

"The vital need of the United States for its own scientific research and for its own drug and chemical industries was brought home to him during the War. From the time his young daughter died, due, he believed, to lack of sufficient technical knowledge in the United States and to lack of essential drugs available in Germany, he labored to bring this country to the point of leadership in scientific industry which it since has attained."

BOOKS RECEIVED

Books received are acknowledged under this heading, and such notice may be regarded as an acknowledgment of the courtesy of the sender. Reviews will be published in the interest of our readers and as space permits.

CUTANEOUS CANCER AND PRECANCER. A Practical Monograph. By GEORGE M. MACKEE, M.D., Professor of Clinical Dermatology and Syphilology and Director of Skin and Cancer Unit, New York Post-graduate Medical School and Hospital, Columbia University, and ANTHONY C. CIPOLLARO, M.D., Associate in Dermatology, Skin and Cancer Unit, New York Post-graduate Medical School and Hospital, Columbia University. With a Foreword by FRANCIS CARTER WOOD, M.D. A volume of 222 pages, with 245 illustrations. Published by The American Journal of Cancer, New York, 1937. Price: $3.75.

DIATHERMY. Including Diathermotherapy and Other Forms of Medical and Surgical Electrothermic Treat-

ment. By ELKIN P. CUMBERBATCH, M.A., B.M. (Oxon.), D.M.R.E. (Camb.), F.R.C.P., Medical Officer in Charge of Electrical Department and Lecturer on Medical Electricity, St. Bartholomew's Hospital. With nine collaborators. Third Edition. A volume of 576 pages, with 168 illustrations. Published by William Wood & Company, Baltimore, 1937. Price: $6.00.

FRACTURES AND DISLOCATIONS FOR PRACTITIONERS. By EDWIN O. GECKELER, M.D., Fellow of the American College of Surgeons, Fellow of the American Academy of Orthopedic Surgeons. A volume of 252 pages, with 213 illustrations. Published by William Wood & Company, Baltimore, 1937. Price: $4.00.

BOOK REVIEWS

ROENTGENATLAS FRUEHTUBERKULOESER VERAENDERUNGEN IM HILUS BEI SYSTEMATISCHEN STANDARDQUERAUFNAHMEN. By DR. R. CZARNECKI, Leiter der Tuberkulose-Abteilung im Staatl. Gesundheitsamt Leipzig-Land. Fortschritte auf dem Gebiete der Röntgenstrahlen, Ergaenzungsband 51. A volume of 98 pages, with 308 illustrations and one plate. Published by Georg Thieme, Leipzig, 1936. Price: 21.60 M.

The author presents a comprehensive report supported by 308 illustrations based upon his systematic observations of disease of the hilus over a period of eight years. The illustrations were chosen from thousands of cases which had been studied by paired postero-anterior and right lateral films of the chest, taken at periodic intervals or in rapid sequence, as the clinical progress demanded, or as research interest indicated.

The purpose of the atlas is to demonstrate that by means of periodic lateral films made under the same conditions involvement and healing of disease of the hilum, with or without involvement of the lung, may be observed and evaluated. The author not only stresses the roentgenologic and technical factors, but also enlarges upon his concept of the biologic-dynamic in the progress of tuberculous infection.

The article should be studied in detail in order to become familiar with the subject matter. The technical factors of position are stressed, especially that covering the right lateral study. The identification of the anatomical structures concerned with the hilum and with the distribution of the bronchial trunks into the lung-fields is well covered. This is followed by detailed discussion of the manner of participation of the hilum lymphatic structures in the various stages of tuberculosis, with emphasis placed on their importance in the primary and secondary stages, in the persistance of tuberculous activity in the glands over many years, and in their rôle as the source of endogenous spread of the disease and of hematogenous dissemination. Several pages are devoted to a discussion of the various phases of the three stages of tuberculosis, and their interrelation. In addition to the usual other methods of treatment, the author has had very satisfactory results with roentgen irradiation over the mediastinum. Small doses are given over one anterior and one posterior field, at intervals of from three to eight or more days, never while there is still a systemic reaction. Irradiation is contraindicated in the presence of active secondary or tertiary lung lesions, since it would interfere with the lymphatic circulation between the active lesion and the regional nodes.

The diagrams and paired illustrations of the author's selected cases are excellently reproduced, and constitute a comprehensive demonstration of the value of these roentgenologic procedures.

DER TUBERKULÖSE PRIMÄRKOMPLEX IM RÖNTGENBILDE: EINE KRITISCHE STUDIE (The Primary Tuberculous Complex in the Roentgenogram: A Critical Study). By DR. J. F. SLOOFF. Number 63, Tuberkulose Bibliothek. A volume of 80 pages, with 61 illustrations. Published by Johann Ambrosius Barth, Leipzig, 1937. Price: 8 M.

In his monograph, "The Primary Tuberculous Complex in the Roentgenogram," Dr. Slooff presents a work valuable to the student of chest diseases. It consists of an introduction; a brief summary and review of the related literature (this is considered from two angles; first, the anatomical, and, second, the roentgenologic); the author's investigations; discussion; observations; summary, and bibliography. The section on the author's own investigations is wisely subdivided into (*a*), discussion of method and technic, and (*b*), detailed case reports of 20 patients of both sexes ranging in age from seven months to twenty-two years.

The work is well illustrated with roentgenograms, descriptive pen-sketches, and post-mortem photographs of the lungs. The whole monograph is well done, with close attention given to important detail and a nice sense of discrimination in choice of material.

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ANEMIA

The Skeletal Changes in the Chronic Hemolytic Anemias (Erythroblastic Anemia, Sickle-cell Anemia, and Chronic Hemolytic Icterus). John Caffey. Am. Jour. Roentgenol. and Rad. Ther., March, 1937, **37,** 293–324.

In these diseases the bone marrow, in attempting an over-production of erythrocytes, becomes hyperplastic and expands, resulting in secondary bone changes. The earliest changes noted have been thickening of the lower portion of the frontal squamosa and horizontal plate, as well as the distal ends of the femora. The heart hypertrophies early; later osteoporosis and heavy trabeculations appear. The vertical striations of the skull and atrophy of the outer table are not as constant as the long bone changes, especially in the metacarpals, which show the expanded marrow, thin cortex, and rectangular outline. Later in the disease the vertical striations disappear to be replaced by osteosclerosis. Mild cases show no definite changes.

The clinical signs antedate by several months the roentgen findings. The heart hypertrophies early. Malnutrition and under-development are present in all cases of early life.

In sickle-cell anemia, the splenomegaly and cardiac hypertrophy are less frequent. Only two-thirds showed thickening, which was limited mainly to the parietal bones. Striations were absent.

Chronic hemolytic icterus shows no definite changes in long bones, and but rarely in the skull.

S. M. Atkins, M.D.

ARTERIOGRAPHY

Pulmonary Arteriography in the Living. Ameuille, G. Ronneaux, Hinault, and H. Desgrez. Bull. et Mém. Soc. Radiol. Méd. de France, February, 1937, **25,** 118–122.

By introducing an urethral catheter 60 cm. long, size 11 or 12, into either the left cephalic or basilic veins it is possible to approach the opening of the vena cava superior into the right auricle. Rapidly injecting 8 to 10 cc. of 120 to 140 per cent sodium iodide and taking roentgenograms immediately, one secures well outlined shadows of the pulmonary arteries. The technic must be meticulous and often it is not possible to introduce the catheter to the proper level. Immediately following the injection there is often transient headache with, occasionally, slight fever or evidence of mild iodism. Otherwise no sequelæ have been noted (75 cases). A second injection (20 grams iodine total) may be given after six minutes if other views are necessary. Tuberculosis is not *per se* a contra-indication.

The angio-pneumograph permits estimation of the distribution and caliber of the (larger) pulmonary arteries throughout their extent.

Parts involved by tuberculosis or abscess show diminution of or loss of vascularity.

Bronchiectasis causes marked change in the distribution of blood vessels. The procedure is frequently unsuccessful in cases of bronchiectasis.

S. Richard Beatty, M.D.

ARTHRITIS

So-called Arthritis Mutilans. J. Schüller. München. med. Wchnschr., Aug. 27, 1937, **84,** 1381.

The author describes six cases of arthritis mutilans, so named by Stursberg, in 1935. The multiplicity of etiologic agents, the lack of uniformity of the microscopic changes, and the lack of microscopic evidence of inflammation in the joints lead him to conclude that this is not a true arthritis, and that the name is a poor one. (Apparently, from his cases, the condition is the one commonly known as neurotrophic osteo-arthropathy here, as two of the cases had spina bifida and two myelodysplasia.)

L. G. Jacobs, M.D.

THE BLOOD

The Effect of Visible and Infra-red Light Emitted by a New Lamp on the Blood Picture of Man. R. Möhring and E. Witte. Strahlentherapie, 1937, **60,** 142.

The authors describe first a new lamp which was used in their experiments and the spectrum of which is very similar to that of the sun. The infra-red rays above 1,200 mμ were filtered out by a water filter. The blood of 50 persons exposed to the rays was studied before and after the treatments. The number of erythrocytes and the percentage of hemoglobin were found increased and the authors conclude, therefore, that undoubtedly a beneficial effect on the blood can be obtained by irradiation from artificial sources of light.

Ernst A. Pohle, M.D., Ph.D.

The Effect of Therapeutic Doses of Roentgen Rays on the Electrolyte Content of Plasma and Erythrocytes in Cases of Basedow's Disease, Leukemia, and Lung Tumor. F. Schmitt and W. Basse. Strahlentherapie, 1937, **59,** 119.

The authors studied the blood chemistry in six patients with Basedow's disease, six cases with leukemia, and ten cases with lung tumors. The latter included carcinoma, sarcoma, and Hodgkin's disease. In Basedow's disease, the potassium and calcium content of the plasma was increased. The chlorine, sodium, and calcium content of the erythrocytes was decreased before irradiation. After irradiation the plasma showed normal values, while chlorine and sodium increased in the erythrocytes and calcium almost disappeared. Potassium and calcium were found increased in the plasma of leukemic patients the same as were the chlorine and potassium content of the erythrocytes, while sodium and calcium values were lower than normal. Following irradiation, chlorine and calcium values were higher in the erythrocytes, the potassium content smaller, with an increase of potassium in the plasma. In patients with malignant lung tumors large doses of roentgen

rays reduced the chlorine in the erythrocytes while the calcium increased. In the spinal fluid of one patient with a tumor of the hilus only one-sixth of the normally present chlorine was found, while calcium was increased 400 per cent.

ERNST A. POHLE, M.D., Ph.D.

BONE DISEASES (DIAGNOSIS)

Osteoporosis Circumscripta of the Skull and Paget's Disease: 15 New Cases and a Review of the Literature. Haig H. Kasabach and Alexander B. Gutman. Am. Jour. Roentgenol. and Rad. Ther., May, 1937, **37,** 577–603.

The disease begins as small, rounded, circumscribed areas of osteoporosis, often in the frontal region near the base, sometimes in the occipital region, occasionally elsewhere. These usually expand to involve almost the entire calvarium. This condition as proven by the literature and the cases of the authors from a follow-up of some years, is a precursor of Paget's disease, though Paget's may occur without this precursor. If Paget's disease is not already present, it will appear later though years may elapse.

Symptoms are usually absent, though headache, vertigo, migraine, and epileptiform attacks may occur. Age incidence is that of Paget's, though the peak age occurs two decades earlier. Occasionally this condition is associated with a bony tumor of the maxillary.

S. M. ATKINS, M.D.

BONES, ROENTGENOGRAPHY

Remarks on Certain Profile Radiographs of Bone. L. Moreau. Bull. et Mém. Soc. de Radiol. Méd. de France, January, 1927, **25,** 49, 50.

The usual position for obtaining profile views of the shoulder joint with the arm in full abduction with the film above and the ray entering through the axilla is often difficult and painful, if not impossible, to obtain. Except rarely, the anterior views are sufficient. To obtain profile views of the head and neck of the humerus it suffices to take views with the arm rotated externally. Profile views of the superior epiphysis of the humerus are obtained when the arm is abducted to right-angles with the hand behind the head.

The usual technics for obtaining profile views of the neck of the femur require positions much too complicated. In the usual position with slight external rotation one obtains a frontal view. To obtain an inside view and define the neck, rotate the leg inward. A profile view of the neck is obtained with the thigh in flexion and abduction. If these views are impossible, stereoroentgenography will suffice.

To obtain, conveniently and without distress to the patient, vertical views of the calcaneus, the patient rests prone with the foot at right-angles to the leg and the toes on the table. The cassette is against the sole, and the central ray is directed obliquely through the heel.

S. RICHARD BEATTY, M.D.

BREAST CANCER

Carcinoma of the Breast. Hugh H. Trout. Surg., Gynec. and Obst., September, 1937, **65,** 370–375.

The author reviewed the histories of 518 cases of carcinoma of the breast, which were seen over a period of 25 years. Some form of dysfunction of the breast was noted in 88 per cent of these histories before carcinoma was found.

The author discusses various theories concerning possible etiological factors in the development of breast carcinoma. Lack of function of the breasts and early interruption of lactation, with failure to remove the products of lactation which may prove irritating, are mentioned as possible factors. He is of the opinion, also, that carcinoma could be "bred out" were it possible to mate human beings biologically as Maud Slye has done with mice.

In the diagnosis of breast carcinoma an attempt is made to obtain a classification of the lesion according to the histological method of grading and also to the clinical index of malignancy as advocated by Lee and Stubenbord. The clinical method of grading is believed to be superior to the histological classification. Routine x-ray examination of the chest, pelvis, and long bones should be made in all cases. In 100 cases of breast carcinoma, the author found five patients with metastases, two of which showed no indication of such lesions before the x-ray examination.

Pre-operative radiation is considered of more value than post-operative therapy. Such improvement is noted in from four to six weeks in many of these cases that the danger exists that some of the patients may fail to return for surgery. A complete Halsted type of operation is performed in every case, if possible. A small stab incision is made in the mid-axillary line and 50 mg. of radium and a light rubber drain are placed in the opening. The drain is placed between the axillary vessels and the radium. An additional 50 mg. of radium is placed in the area supplied by the internal mammary vessels and lymphatics. Four 12.5 mg. radium needles are equally distributed in a rubber tube from 12 to 15 inches long. The tube is placed under the skin and the long end brought out through the lower end of the incision. The author states: "We have never been able to detect how the radium in any way seems to interfere with the healing of the incision or the 'taking' and development of the skin grafts." Post-operative radiation has been found to produce bronzing of the skin, especially in the area previously irradiated by radium. The author believes that an artificial menopause by irradiation of the ovaries should be done in every case in which the patient is still menstruating. Metastases also are irradiated because of the increase in comfort obtained by the patient.

The statistics presented prove the value of radiation therapy and radical surgery in the treatment of carcinoma of the breast. Up to 1920, radical surgery alone was employed and the five-year "cures" were 22 per cent. From 1920 to 1924, radium was added

to radical surgery and the five-year "cure" rate of this period was 30 per cent. Since 1924, pre-operative and post-operative therapy have been added to radium and radical surgery and the five-year "cure" rate has been increased to 55 per cent. Of interest also is the fact that only one local recurrence has been noted in 117 patients irradiated before surgery, while the non-irradiated group previously had local recurrences in slightly over 5 per cent.

J. N. Ané, M.D.

THE CRANIUM

The Reliability of the Roentgenographic Signs of Intracranial Tumor. Merrill C. Sosman. Am. Jour. Roentgenol. and Rad. Ther., December, 1936, **36,** 737–743.

Sosman states that "one's relative value in assisting the often long and involved course leading to a correct diagnosis is in inverse ratio to the clinical experience and judgment of the physician referring the patient" (a statement relating particularly to the author's chosen subject but equally applicable to any major diagnostic problem).

The writer's comments are based upon the x-ray findings of all cases referred for skull study from both the neurosurgical and medical services for a period of one year. Positive findings were grouped as showing: (1) non-specific signs of intracranial tumor, (2) localizing signs, and (3) characteristic signs permitting identification of the type of tumor.

An interesting observation obtained from analysis of the cases examined from the medical service of the hospital is that one may expect to find about one brain tumor case per 100 medical admissions, since 26 cases with 18 subsequently verified by the neurosurgical service were found in 1,900 hospital admissions. Further analysis of the material supplied by the medical service revealed slightly greater accuracy of the x-ray examination (without encephalography and ventriculography) than by clinical examination "by a group of medical men not particularly brain-tumor-conscious." To his considerable surprise the writer found that in the present series, by plain radiographic studies, he was able to predict the location of the tumor in about one-half of the cases and to guess its histologic type in one-fourth of the group. Concerning percentage accuracy in localization in the verified group, it was found that with pituitary adenomas the accuracy was 91 per cent, meningiomas 67 per cent, acoustic neuromas (confirmed by x-ray) 53 per cent, cerebellar tumors (compatible, not diagnostic) 45 per cent, gliomas 28 per cent.

The most valuable view for the study of the acoustic neuroma is the direct anteroposterior view showing the petrous ridges in the center of the orbits.

The position of the silver clips used for hemostasis is important to note in re-examining for recurrence or for the results of roentgen therapy.

If ventriculography is resorted to, practically all intracranial tumors of sufficient size to produce symptoms should be correctly treated.

J. E. Habbe, M.D.

CYSTS, CUTANEOUS

Recurring Myxomatous, Cutaneous Cysts of the Fingers and Toes. Robert E. Gross. Surg., Gynec. and Obst., September, 1937, **65,** 289–302.

The author discusses the results of his study of myxomatous, cutaneous cysts of the fingers and toes, reviews 14 cases of this condition reported in the literature, and presents eight additional examples. This rather rare lesion was described by Jones and Markins and later by Hyde.

In the author's series the cysts varied from 5 to 12 millimeters in diameter and consisted of smoothly rounded, thin-walled structures of the color of normal skin or with a faint yellowish or bluish cast. Tenderness is mild or absent. The cyst is found only on the dorsal surface of the digit, usually in the proximity of a joint.

Pathologically, the cysts show a degeneration or resorption of the collagen in a localized area of the derma. The fibroblasts remain in a framework with but little intracellular material. Between the separated cells there then collects a faintly staining, basophilic, mucoid material which increases in amount. The fibroblasts then disappear and minute cavities appear. The increase in number and size of the cavities results in a grossly visible cyst containing a clear and glairy fluid of gelatinous consistency. No communication with a subjacent structure, such as a joint cavity, tendon sheath, or bursa has been noted. The mucoid material is, therefore, the result of degeneration of local connective tissue.

While the pathogenesis of cutaneous cysts is unknown, two theories are presented. The first theory is based on degenerative processes set up by local trauma. The second explanation is that the cysts result from localized alteration of blood supply. While these have been called "synovial lesions," the basis is without foundation for there is no connection with any of the synovial membranes. The idea of neoplasia can also be eliminated for the pathological findings are those of a degenerative and not a neoplastic lesion.

The treatment of choice in cutaneous cysts is radiation therapy. All types of surgical therapy, such as drainage, excision, curettage, and insertion of sclerosing fluids are of no avail. The author employed x-ray therapy in six cases, using in each, 600 r given in two doses of 300 r each, two days apart. In five lesions there was no recurrence, but in one case an additional 960 r was given. Sutton used 10 mg. of unscreened radium and a dosage of 40 milligram-hours in one patient. In the author's opinion an intense local reaction must be produced in order for the treatment to be effective.

J. N. Ané, M.D.

GONORRHEA

Experimental Studies Regarding the Possibilities of the Use of Alpha Rays in the Treatment of Gonorrhea. H. Nagell and W. Noethling. Strahlentherapie, 1937, **59,** 419.

The authors studied the bactericidal effect of alpha rays on gonococci *in vitro*. If the surface of cultures was exposed to alpha rays, it required from 4 to 60 alpha particles per μ^2 to kill about 95 per cent of the cocci. In a liquid medium it required the energy of from 0.01 to 0.4 alpha particles per μ^3 of liquid medium to produce the same effect. Similar experiments were conducted with thorium-X solutions and also with polonium.

The authors conclude that ointments containing about 0.02 to 0.2 mc. per c.c. of radium emanation should be of practical use if applied for several hours per day.

ERNST A. POHLE, M.D., Ph.D.

Treatment of Gonococcal Arthritis with Radio-active Substances. P. Loup. Jour. d'Urol., March, 1937, **43,** 238–240. (Reprinted by permission from British Med. Jour., July 10, 1937, p. 6 of Epitome of Current Medical Literature.)

The author refers to the serious complications, reported by Dr. Marsan, which have followed the introduction of radio-active substances, particularly when intravenous injections of thorium-X have been given, in cases of gonococcal arthritis. Anemia has sometimes resulted, and in one instance a patient developed an osteosarcoma of the right femur, from which he died, several years after intravenous injections of thorium-X had been given. Two personal cases are reported in which this treatment was successful and without complications up to the present. In the first a young man, 19 years of age, was suffering from a severe attack of gonorrhea which was affecting the joints of the hand. A subcutaneous injection of anti-gonococcal serum was given with success. The patient attended only irregularly and returned after several days with severe arthritis of the right knee, which was swollen, painful, and useless. Further injections were given and local treatment applied, but the condition of the knee became steadily worse. Intravenous injections of a solution of thorium-X were given, and the knee, which had been ankylosed before the injections began, soon could be flexed to a right-angle, and after three months movement was completely normal. Seven years later the patient was in perfect health with no disability of the knee-joint. In the second instance a woman, 28 years of age, had been receiving an intravenous injection of "gonocrine" every other day, but in spite of this a typical arthritis developed in the wrist with a synovitis of the right thumb. Anti-gonococcal serum was given daily without any effect on the arthritis, and so injections of the same solution of thorium-X were tried, with the same good result as in the former case. After three years the patient was still in good health. The danger of this form of treatment as emphasized by Dr. Marsan is a strong deterrent to its universal use.

GYNECOLOGY AND OBSTETRICS

The Value of a Supine Lateral Roentgenogram as an Obstetrical Guide. H. Reichenmiller. München. med. Wchnschr., Aug. 6, 1937, **84,** 1254.

The author takes a lateral view of the pelvis with the patient supine, and on it measures the conjugata vera. He corrects for distortion by measuring the focus-film distance (h'), and the distance to the mid-point of the patient at the level of the trochanters (h), which is equal to h'—half the intertrochanteric width. Then the measured conjugata vera, A', is corrected to the true conjugata vera, A, by the equation $A = \frac{h}{h'} A'$. A table showing the comparison with clinical and anatomical measurements is given. The dose of radiation under the conditions he uses is from 9 to 12 r per plate.

Deformities of the pelvis cause difficulty in securing satisfactory measurements, but not more than they do clinically. For satisfactory measurement, plates must clearly show the back of the symphysis, the femur, and the sacrum. The femora and acetabula should be concentrically projected, and centered on the Bucky (which is a rotary grid in his clinic).

Information on the position, height, and configuration of the fetal head is also made available at the same time. The indications for the examination, mentioned at some length, are very broad, since no harm can possibly result from it. In certain circumstances it may replace vaginal examination.

L. G. JACOBS, M.D.

The Time Factor and Tolerance Doses with the Protracted Dose Method in Gynecology. Th. C. Neeff. Strahlentherapie, 1937, **60,** 152.

Many years of clinical observation and careful physical measurements have led to the development of the following technic in treating cancer of the uterus by roentgen rays and radium in the Women's Clinic of the University of Wurzburg; 14 abdominal and 10 sacral fields are used, one field per day. The surface dose is 300 r given in 60 minutes over an area of 400 cm.^{2}. The total dose over the abdomen is 4,500 r and the one in the depth is 3,400 r. To these roentgen doses a maximum of intra-uterine radium of 5,000 mg.-hr. is added, requiring approximately 27 days for the entire series of treatments. The radium tolerance dose at 1 cm. distance for the rectum is 6,200 r, for the bladder, 6,600 r, for the vagina 15,400 r. In conclusion the author emphasizes again the necessity of accurate dosage.

ERNST A. POHLE, M.D., Ph.D.

Diagnosis and Treatment of Tuberculosis of the Female Genital Organs. F. Gal. Strahlentherapie, 1937, **59,** 513.

The author reports his experience in the treatment of tuberculosis of the female genital organs with roentgen rays in a series of 23 cases out of a total number of 79 and compares the results obtained by radiation with those following operation. The majority (42) of the

patients had tuberculosis of the tubes. Twenty-two of the irradiated women were treated with roentgen rays alone, one with radium exclusively, and three were treated with the combined method. As a rule, small doses were given; most patients received one third of the sterilization dose for four or five sittings at intervals of from four to five weeks. The appearance of the menopause is usually followed by an improvement in the condition of the patient; amenorrhea is, therefore, considered beneficial in the treatment of these cases. All irradiated women had some form of surgery, so that the diagnosis had been verified histologically in each instance. The results of radiation therapy were encouraging; in localized processes the end-results following operation and irradiation were about the same. The author states, however, that in early cases with limited involvement removal of the adnexa or vaginal hysterectomy is the method of choice because of assured results. Tuberculosis limited to the cervix can be treated successfully by radium without danger. The same holds true of tuberculosis of the uterus if there are contra-indications to surgery.

ERNST A. POHLE, M.D., Ph.D.

The Drinking Fetus. K. Ehrhardt. München. med. Wchnschr., Oct. 22, 1937, **84**, 1699, 1700.

In a 21-year-old woman, pregnant six months, eugenic sterilization and abortion was done. Before the operation the author replaced 8 c.c. of amniotic fluid with colloidal thorium dioxide. The operatively removed specimen consisted of the fetus and membranes intact. Roentgenograms of this, of the fetus alone, and of the fetal gut all showed thorium dioxide in the gut. The author concludes that the fetus normally swallows significant quantities of amniotic fluid. He briefly mentions some of the possible applications of this fact.

L. G. JACOBS, M.D.

Roentgen Pelvimetry and Fetometry. Paul C. Hodges. Am. Jour. Roentgenol. and Rad. Ther., May, 1937, **37**, 644–662.

A review of the recent publications in this field and the author's own work lead to the fact that no single method has been accepted as standard and opinion varies on what information should be sought. There is a growing recognition of the importance of a qualitative survey of the pelvis as a whole, that is, whether of the gynecoid, android, anthropoid, or flat type, the subpubic angle and other factors enumerated by Caldwell and Moloy rather than the diameters alone.

Of the three methods now employed: (1) the position, (2) stereoscopic, (3) the one introduced by Ball and Marchbanks, the multiple stereoscopic views method is the one of choice, but owing to the simplicity and inexpensiveness of the Ball and Marchbanks' method, which the author suggests calling "90° triangulation," he believes the latter will be increasingly employed. To overcome the objections of possible movement of the skull during the examination, the author has devised a jacket in which the patient is strapped, and for Ball and Marchbanks' method of correction of triangular distortion, he has substituted equations and graphs based on definite sound mathematics.

S. M. ATKINS, M.D.

THE LUNGS

Bronchography as an Aid in the Diagnosis of Carcinoma of the Lung. Max Cohn. Le Cancer, 1935, **12**, 251–258.

In most cases carcinoma of the lung originates in the bronchi, and the radiologic diagnosis depends on indirect evidence, due primarily to complete or partial occlusion of the bronchus, atelectasis or retention of secretion. Consequently, the radiologic study is frequently negative, especially in the early stages of the disease or if the tumor is in one of the smaller bronchi.

The technic of bronchoscopy as developed in America permits not only direct visualization but also the directed filling of the bronchi with iodized oil. This is accomplished without distress to the patient by preliminary anesthesia of the lower respiratory tract.

Bronchography with the aid of opaque oil has made possible visualization of the suspected area from all directions, and aided in determining the site of occlusion not visible on plain roentgenograms in the upper as well as the lower lobes. The lateral and oblique views are indispensable.

S. RICHARD BEATTY, M.D.

Roentgen Evidence of the Behavior of the Human Lung in Recent Tuberculous Infections. Kenneth D. A. Allen. Am. Jour. Roentgenol. and Rad. Ther., May, 1937, **37**, 603–612.

Both animal experimentation and serial roentgen examination of human patients show that first infection tuberculosis of lung parenchyma is quickly carried away to the hilum, but that subsequent infections remain where the infection occurs. In the serial examinations the original parenchymal involvement was seen to subside rapidly, during which time the hilum became enlarged and hila glands appeared, to be in turn followed by only a Ghon tubercle in the parenchyma and calcification in the hilum as a monument to this first infection. A subsequent parenchymal infection remains in the parenchyma without drainage to the hilum.

S. M. ATKINS, M.D.

When is Roentgen Investigation of the Lungs Necessary? Balder Kattentidt. München. med. Wchnschr., Oct. 15, 1937, **84**, 1647–1652.

The author concludes from certain statistics that he found rather fewer patients with tuberculosis among those presenting symptoms than among those symptom-free, and that a roentgenogram of the chest is essential to the early diagnosis of lung tuberculosis even in the face of a negative history. The article contains some discussion of the stand of the German National Tuberculosis Committee and the *Krankenkassen* on the subject.

L. G. JACOBS, M.D.

RADIATION INJURIES

Clinic and Therapy of Professional Injuries Due to Roentgen Rays. F. F. Freund. Strahlentherapie, 1937, **58,** 694.

The author briefly reviews the history of roentgen injuries occurring in individuals who come in contact with them professionally. The first typical symptom of a chronic roentgen poisoning is a drop in the leukocytes with a relative increase in the lymphocytes. The prognosis is usually good if the changes are recognized early and if complete protection from radiation from then on is afforded. The treatment consists of physical exercise and sojourns in higher altitudes. Arsenic and pyramidon are contra-indicated.

ERNST A. POHLE, M.D., Ph.D.

Injuries Following "Bucky" Irradiation. F. Kalz. Strahlentherapie, 1937, **59,** 547.

The assumption of Bucky that skin injuries of a serious nature will not occur if very soft roentgen rays (Grenz) are used, is not correct. Although there have been no ulcers described during a period of 15 years, changes like atrophies and telangiectases have been observed by a number of radiologists. Depending on the penetration of the radiation, these skin injuries will occur after doses of from 1,600 (H.V.L. 0.034) to 4,000 r (H.V.L. 0.016). There also seems to be a difference in sensitivity in different parts of the body. Highly sensitive are the eyelids and surrounding parts as well as the lateral cervical areas. The author then reports five cases showing late injuries after Grenz-ray exposure, consisting of telangiectasis, depigmentation and one case with pigmentation as seen in lentigo. The conclusion, therefore, is obvious: Accurate determination of the dose and careful observation of the upper safe limits are indicated.

ERNST A. POHLE, M.D., Ph.D.

Radiation Tumors. Hans Hellner. Münchin. med. Wchnschr., June 18, 1937, **84,** 980–984.

While human radiation cancer is in some sort an experimental cancer, similar lesions in laboratory animals are rather infrequently reported. The author notes a decline in reported human cases, especially when the increased use of x-ray is considered. The time from first irradiation to a diagnosis of cancer is about ten years. Every case was frequently and heavily irradiated, usually by several physicians. The author's cases are briefly described as to location and treatment.

The author feels that the tumor theory of Bernhard Fischer-Wasels best explains roentgen carcinoma. Roentgen sarcoma is rarer than roentgen carcinoma, and often occurs after continued intensive irradiation of joint tuberculosis. As a rule it occurs from five to seven years after the irradiation. The tuberculosis has apparently a secondary etiological rôle. The epiphyses were especially sensitive, and histologically the tumors in his cases were osteochondrofibrosarcomas. He reports a case of roentgen sarcoma occurring in the hand after irradiation eleven years previously for joint tuberculosis.

Experimental radium sarcomas of the soft parts have long since been recognized, workers undertaking to produce such tumors in the lower end of the femur of rabbits. Success resulted in one case with repeated doses of radium over two years to the knee. The author feels that these facts should lead to caution in the irradiation of joint tuberculosis and of other conditions in the epiphyseal, especially of the knee.

L. G. JACOBS, M.D.

How does Necrotic Roentgen Ulcer Develop? B. Dahl. Strahlentherapie, 1937, **59,** 522.

The pathogenesis of the roentgen ulcer is not known. The author studied, therefore, the skin reaction in rats and frogs histologically, following the application of destructive doses of roentgen rays (3,000–4,000 r). He concludes that in the development of the roentgen ulcer two different factors must be recognized: the direct injury of the cells and the subsequent secondary reaction in the blood vessels. The edema in the capillaries hinders the blood circulation in the connective tissue which will, therefore, undergo necrosis. This process may continue and extend into deeper layers of tissue. Regeneration and repair will take place only if the connective tissue and blood vessels regain their faculty to form granulation tissue.

ERNST A. POHLE, M.D., Ph.D.

Radiation Cancer in Radiologists. A. Béclère. Strahlentherapie, 1937, **60,** 9.

This is the first paper in Volume 60 of "Strahlentherapie," which is dedicated as "Festschrift" to its editor, Prof. H. Meyer, of Bremen, in honor of his sixtieth birthday. The Nestor of the French radiologists discusses the changes occurring in the skin of radiologists following continued and excessive exposure to radiation. His article closes with a note of warning: Do not underestimate the seriousness of even early changes in the skin because carcinomatous degeneration sets in early and the sooner these lesions are radically removed the better is the chance for a cure.

ERNST A. POHLE, M.D., Ph.D.

THE SPINE

Perirenal Insufflation. Aubry and Bertrand-Guy. Bull. et Mém. Soc. Radiol. Méd. de France, February, 1937, **25,** 133–135.

The classical method of approach for insufflation of the perirenal capsule is to place the needle from 15 to 20 mm. before, below, and to the side of the transverse process of the second lumbar vertebra.

The authors employ the same technic as for splanchnic anesthesia. With the patient seated, the needle is introduced at the lower border of the twelfth rib, 7 cm. from the midline on the right, 4 cm. on the left, inclin-

ing the needle 45 degrees toward the midline, aiming at the vertebral body and feeling the way until the needle enters soft tissue that offers no resistance. From 300 to 400 c.c. of air is introduced with a pneumothorax apparatus. The method is no more difficult than lumbar puncture.

S. RICHARD BEATTY, M.D.

Accessory Articular Processes in the Lumbar Spine. Harry L. Farmer. Am. Jour. Roentgenol. and Rad. Ther., December, 1936, **36,** 763–767.

In a series of 2,535 x-ray examinations of the lower spine, 40 cases, or approximately 1.5 per cent, showed accessory articular processes. In the 40 cases there were 60 such anomalies in all, a number of cases showing bilateral involvement or involvement of several vertebræ. Most commonly the second and third lumbar segments were affected although some cases were found involving the first, fourth, and fifth segments. The vast majority were of the inferior articular facets although there were five instances of superior articular process anomaly.

J. E. HABBE, M.D.

A Case of Calcification of the Abdominal Aorta. Dumolard, Bertrand-Guy, Tillier, and Porot. Bull. et Mém. Soc. Radiol. Méd. de France, February, 1937, **25,** 136, 137.

In a woman 50 years of age marked calcification of the abdominal aorta in conjunction with an advanced hypertrophic arthritis of the spine with decalcification of the lumbar bodies was demonstrated radiographically. The authors speculate as to the rôle of the parathyroid in such disturbances of calcium metabolism.

S. RICHARD BEATTY, M.D.

SUPRARENALS

Radiotherapy of Suprarenals in Endarteritis Obliterans. Desplats and Langeron. Jour. d. Radiol. et d'Électrol., April, 1937, **21,** 152, 153. (Reprinted by permission from British Med. Jour., June 26, 1937, page 103 of Epitome of Current Medical Literature.)

The authors have treated the adrenals with x-rays in 200 cases of obliterating endarteritis, and claim good results in 62.5 per cent and improvement in 22.5 per cent; only 5 per cent failed to respond to the treatment. Diabetic endarteritis seemed to respond to the treatment in almost every case. They used 130 kilovolts filtered through 5 to 7 mm. of aluminum, 150 to 250 units to each adrenal region alternately every second day until improvement set in. They find that it may be necessary to continue the treatment for one, two, or even three months with short breaks between each series of six treatments. In a few cases of intermittent claudication treated in this way the cure has been maintained for seven or eight years.

SYPHILIS

The Sedimentation Test in Tuberculosis and Syphilis. F. Scheidemandel. Deutsches Tuberk.-Bl., March, 1937, **11,** 69–72. (Reprinted by permission from British Med. Jour., May 1, 1937, page 72 of Epitome of Current Medical Literature.)

The author has found in an institution serving as a clearing station for definite and doubtful cases of tuberculosis that the rate of sedimentation of the erythrocytes is a valuable guide to differential diagnosis, although this test is not specific but is merely indicative of inflammatory and destructive changes in the body. He gives details of four cases common to which were little or no radiological evidence of active pulmonary tuberculosis, doubtful clinical signs of it, a negative intracutaneous tuberculin reaction, a positive Wassermann reaction, and a remarkably high rate of sedimentation. The contrast between this high rate and the negative findings on radiological and physical examination of the chest was striking.

This experience has taught the author to require a Wassermann test whenever the findings of the sedimentation test could not be accounted for by reference to pulmonary tuberculosis; and in the course of the last two years he has, by taking this precaution, been able to provide anti-syphilitic treatment for 17 patients the nature of whose disease had not previously been recognized. A rapid rate of sedimentation may well be due to untreated secondary syphilis, whereas in tertiary syphilis this rate is comparatively slow. Indeed, it is almost normal in latent forms of syphilis in which the Wassermann reaction is negative. When it is positive, but the syphilis is latent, the sedimentation rate is only slightly raised. When a tuberculous process is slight and scarred and is not calculated to have any effect on the rate of sedimentation, a high rate should raise suspicions of Wassermann-positive syphilis running a more or less latent course.

Studies in Cardiovascular Syphilis: Teleroentgenography in Diagnosis of Early Syphilitic Aortitis: Comparison of Findings in 1,000 Syphilitic and 600 Non-syphilitic Individuals. J. E. Kemp and K. D. Cochems. Am. Heart Jour., March, 1937, **13,** 297–307. (Reprinted by permission from British Med. Jour., June 26, 1937, page 103 of Epitome of Current Medical Literature.)

The authors, in an attempt to evaluate teleradiographic measurements in uncomplicated early syphilitic aortitis, have compared the teleradiographs of the heart and aorta in 1,000 cases of unselected syphilitics with those of 600 unselected non-syphilitic individuals of the same occupational, sex, and age groups. The Vaquez-Bordet measurements of the supracardiac shadow were used in comparing the width of the aortic arch. Only 59 per cent of patients with clinically recognizable syphilitic aortitis showed teleradiographic evidence of aortic dilatation, but there was no evidence that the diagnosis of uncomplicated syphilitic aortitis can be made by teleradiography alone.

THE THYROID

Roentgen Treatment of Exophthalmic Goiter. O. Raagaard. Ugesk. f. læger, April 29, 1937, **99,** 453–459. (Printed by permission from British Med. Jour., June 26, 1937, p. 103 of Epitome of Current Medical Literature.)

The author draws attention to the lack of unanimity as to the respective merits of radiological and other treatment for Graves' disease. Of late in Denmark the value of radiological treatment has been much underestimated, as the impression that it is more or less an unessential supplement to medicinal treatment is widespread. The author has conducted a follow-up study of 68 definite cases which were given radiological treatment, ambulatory in most cases, between 1922 and 1933 in a Danish hospital. The disease was severe in six cases, moderately severe in 26, and mild or slight in 36. An observation period of from three to eleven and a half years was counted from the conclusion of treatment. In 57 cases the follow-up study included a medical examination. Recovery could be claimed in 70.6 per cent, and almost complete recovery in 7.4 per cent. The improved represented 10.3 per cent, while 7.4 per cent were unchanged. There was one death from Graves' disease in addition to two deaths from other causes. In 85.3 per cent complete fitness for work was found on re-examination, and 5.9 per cent were partially fit. No patient was refused radiological treatment or found to be refractory to it. In 64 per cent the goiter disappeared completely. The average duration of treatment was 11.9 months, and the average number of exposures was 7.3. The author's comparison of his experiences with those of radiologists in other countries reveals a certain uniformity in the results achieved. He concludes that radiological treatment produces as good results as does operative therapy.

Malacia of the Neck of the Femur with Combined Degeneration of Hypophysis and Thyroid. R. Kienböck. Strahlentherapie, 1937, **60,** 115.

The author reports a case of a man 54 years old, who was admitted to the hospital in 1936. During the last 14 years he had been steadily gaining weight and recently developed dizziness and nausea, with difficulty in walking. At the age of 13 he had a thyroidectomy. The clinical diagnosis was myxedema. Roentgen examination of the hips showed a bilateral juvenile malacia of the neck of the femurs, apparently on the basis of an endocrine dysfunction. The patient died from gangrene of the lung shortly after admission. The autopsy revealed myxedema of the entire body, operative defect of the thyroid, and hypoplasia of the hypophysis. The changes shown in the roentgenogram in both hip joints were verified. The author believes that we have to deal with a combination of two types of degeneration produced by endocrine dysfunction, namely, partial infantilism and degeneration of the skeleton on a hypophyseal basis.

ERNST A. POHLE, M.D., Ph.D.

TUBERCULOSIS, PULMONARY

The Problem of Tuberculosis. B. P. Potter. Jour. Am. Med. Assn., May 8, 1937, **108,** 1585–1590.

This is an address presenting this problem from the general practitioner's point of view. It is apparent that the finding of frank cases of tuberculosis can be enhanced only by methods of greater precision and by the utilization of a more extensive case-finding program. The wider use of the x-rays and less attention to physical examinations in all patients who consult physicians for symptoms that even in the remotest way suggest the possibility or probability of tuberculosis will be a great step forward.

The practitioner has a part to play in the examination of contacts of the known cases of tuberculosis, and as an educator in the larger plan of case-finding of individuals with asymptomatic tuberculosis. His influence must be extended to include proper management of the open case, with two things in mind: first, to segregate the patient and, second, to convert the sputum abacillary by early treatment at home or in the office of those in whom this is possible.

The physician must realize that the earlier appropriate therapeutic measures are applied the sooner the patient ceases to be a menace, and the prognosis becomes increasingly more favorable in many instances.

CHARLES G. SUTHERLAND, M.D.

Tuberculous Tracheobronchitis. Paul C. Samson, John Barnwell, John Littig, and John C. Bugher. Jour. Am. Med. Assn., May 29, 1937, **108,** 1850–1855.

Since patients whose pulmonary tuberculosis is complicated by tuberculous tracheobronchitis have a relatively grave prognosis, the clinical recognition of this complication should be of concern to all phthisiotherapists. They define the condition as a specific infection of the mucosa or submucosa of the trachea and bronchi and to be distinguished from "tracheobronchial tuberculosis" which signifies clinical tuberculosis of the tracheobronchial lymph nodes.

The predominant mode of mucosal infection appeared to be direct contact with tubercle bacilli from pulmonary cavities. Microscopically the primary tracheobronchial lesions were either minute ulcers in the mucosa or small tubercles presumably resulting from the deposition of tubercle bacilli in the crypts of mucous glands. With progression of the lesions there were submucosal infiltrations with overlying intact mucosa showing edema and congestion or varying degrees of mucosal ulceration. The lesions were characteristically on the posterolateral walls of the bronchi and trachea, further suggesting implantation infection. Occasionally a direct massive extension from a pulmonary cavity to the peribronchial tissue was observed, with subsequent involvement of the mucosa.

As far as the bronchi were concerned, only about one-third of the cases showed evidence that was consistent with a mucosal involvement secondary to tuberculous infection of the peribronchial lymphatics. Out of 49

patients in whom a bronchoscopic diagnosis of tracheobronchial disease was made, nearly one-half showed no evidence of active laryngeal tuberculosis.

Roentgenographic evidences include: (1) The appearance of intermittent areas of atelectasis in serial roentgenograms of the chest. (2) Sudden lobar collapse following a paralysis of the hemidiaphragm or the induction of pneumothorax. (3) The visualization of tracheal or bronchial narrowing, particularly in studies made with the Potter-Bucky diaphragm. (4) The occasional demonstration of bronchial stenosis beyond the limits of bronchoscopic vision by brominal bronchograms. This method of examination has occasionally been useful when the bronchoscopic examination was negative in the face of strong presumptive clinical evidence of tuberculous tracheobronchitis. They used bronchoscopy to confirm the suspected presence of tuberculous tracheobronchitis. Four types of lesions are recognizable: the findings are described in detail. Roentgen therapy was used on a series of cases; a critical evaluation of results was not yet justified.

CHARLES G. SUTHERLAND, M.D.

Some Roentgen Considerations of the Childhood Type of Tuberculosis. Earl E. Barth. Illinois Med. Jour., October, 1937, **72,** 328–330.

Barth concludes that "(1) The proper interpretation of a roentgenogram of the chest of a child having tuberculosis requires a knowledge of the pathology as well as of the anatomy and physiology of the lung; (2) a roentgen study of the chest is indispensable in the examination of a child suspected of having tuberculosis; (3) the physician who interprets the films should have, or be given, a statement regarding the history, physical findings, and the result of tuberculin test if available; (4) serial films will yield more definite information than a single examination and will help to rule out nontuberculous lesions, and (5) two types of lesions should be looked for: the parenchymal and the tracheobronchial. Pleural effusion, atelectasis, and obstructive emphysema will be found in some instances."

G. E. BURCH, M.D.

TUMORS (DIAGNOSIS)

Traumatic Localization of a Tumor Metastasis (?). M. Richard. Schweiz. med. Wchnschr., July 10, 1937, **67,** 649, 650.

A case report of a man in whom an injury to the wrist seemed to lead to the localization there of a hypernephromatous metastasis (primary not found). The further study of the case showed, however, that the metastasis must have been present before the injury.

L. G. JACOBS, M.D.

Microscopic Grading of Tumors: Its Interpretation, Limitations, and Relation to Radiosensitivity. William Carpenter MacCarty. Am. Jour. Roentgenol. and Rad. Ther., March, 1937, **37,** 365–367.

Microscopic grading and sensitivity conclusions must not be drawn prematurely, for there is no microscopic grading or classification which has absolute value in clinical prognosis, even though Broders' grading will lead to fewer errors. In each tumor there are to be considered lymph node involvement, fixation, size and duration of growth, anatomical location, renal and cardiac efficiency, absence of anemia, lymphocytic infiltration, fibrosis, hyalinization, and cellular differentiation.

S. M. ATKINS, M.D.

An Apparently Solitary Myeloma. P. Grüneis. Röntgenpraxis, March, 1937, **9,** 190–192.

Multiple areas of bone destruction are typical of myelomas. Single solitary myelomas have been described in the literature only rarely. The diagnosis of multiple myeloma is at times quite difficult, especially its differentiation from carcinomatous metastases. When only a single myelomatous area of bone destruction is shown, the diagnosis is still more difficult.

In the author's case a roentgenogram of the chest showed a well circumscribed area of increased density in the base of the right chest and a tumor mass which surrounded an area of destruction in the seventh rib, which was well localized and cystic. The roentgen diagnosis was metastatic carcinoma or myeloma. At autopsy it was found that the lesion was a plasma-cell myeloma with a few other very small foci in the skull and sternum which were not shown radiographically.

HANS W. HEFKE, M.D.

The Differential Diagnosis of Mediastinal Tumors. N. Lloyd Rusby. Proc. Roy. Soc. Med., Sect. Med., August, 1937, **30,** 1205–1208.

Rusby points out that in the differential diagnosis of mediastinal tumor, a detailed radiological examination is of greatest service. This includes postero-anterior, lateral, and oblique views of the chest as well as fluoroscopic screening. Contrast media, such as lipiodol, are often useful. The possibilities of radiological examination are not yet exhausted. Such an examination can be combined with certain other procedures to elicit facts of the greatest value, such as the introduction of artificial pneumothorax to show the relationship of the mass to the pleural space and whether it lies within or outside of the lung substance. Introduction of air into cystic tumors has aided in their differentiation from pleural fluid.

W. A. SODEMAN, M.D.

TUMORS (THERAPY)

Radiotherapeutic Experiences in Malignant Tumors of the Upper Respiratory and Digestive Tracts with Regional Lymph Node Involvement. A. Pagani. Strahlentherapie, 1937, **59,** 575.

The author reviewed 150 cases of tumors of the mesopharynx observed during the period from 1929 to 1935 at the Roentgen Institute of Schinz. The localization

was as follows: soft palate 10, tonsils 49, base of tongue 32, angle of jaw 16, valleculæ 22, mesopharynx wall 21 cases. Of the tonsil tumors, 38 were carcinomas and 11 sarcomas. Only 24 of all patients admitted were operable. The histology of these neoplasms and also some of the clinical features are discussed. In two comprehensive tables a synopsis of all treated cases and the end-results are given. Photographs of a few illustrative cases are appended.

The method of choice in treating the primary tumor as well as the regional lymph glands is protracted fractional roentgen therapy applied with low intensity. The tumors of the soft palate without metastasis may be seeded or treated by radon molds. Small residual tumor masses or local recurrences are treated with radium or are destroyed by electrocoagulation. If there is any residual glandular involvement after roentgen therapy, the glands are removed provided that the primary tumor has been completely eradicated. Primary resection of the lymph nodes is not recommended. Of all cases with tumors of the mesopharynx plus glandular metastasis, 25 per cent remained well for three years and 21 per cent for five years. The final outcome depends entirely on the stage of the disease when treatment is started and also on the metastases; consequently, the results can be improved only if these cases are diagnosed early.

ERNST A. POHLE, M.D., Ph.D.

Radiation Therapy of Malignant Tumors. R. du Mesnil de Rochemont. Strahlentherapie, 1937, **60**, 120.

The success of radiation therapy of tumors depends on the stage of the disease, its localization, the character of the tumor, and proper and adequate radiation technic. The rôle of the time factor in radiation therapy has been discussed in detail during the last few years and undoubtedly valuable information has been gained. Homogeneous distribution of the dose in the entire diseased area is of the greatest importance and the author analyzes the factors which influence it. The advantages and disadvantages of the use of very short focal skin distances are also discussed.

ERNST A. POHLE, M.D., Ph.D.

Endometrioma. M. Rocmans and Petitfrère. Bruxelles med., May 2, 1937, **17**, 1001–1006. (Reprinted by permission from British Med. Jour., July 31, 1937, p. 20 of Epitome of Current Medical Literature.)

The authors define an endometrioma as a tumor which possesses the characteristics of endometrium but which occupies an abnormal position. It occurs most often in young women and may be situated in various regions. Two cases are reported, in one of which the tumor was on the upper part of the broad ligament, and in the other it was adherent to the recto-vaginal septum. In the first case the patient had suffered from pain in the right iliac fossa for four years. This pain, which radiated to the right hip and the lumbar region, became severe enough to necessitate operation. A tumor the size of a large nut was removed from the broad ligament, and was found on microscopical examination to have the characteristics of an endometrioma. In the second case the patient had complained of indigestion for three years, particularly at her menstrual periods, with vomiting and lumbar pain. Appendectomy, together with the removal of the left adnexa, was carried out, and a small cystic nodule was felt in the pouch of Douglas but was not removed owing to adhesions. A year later this tumor had grown and was adherent to the posterior vaginal wall and the adjacent tissues. There were symptoms of tenesmus and some menstrual irregularity. A posterior colpotomy was performed, which gave access to the tumor. It was found to be an endometrioma, but was too adherent to be removed.

Two tubes of radium were inserted, and a month later menstruation became normal, the symptoms disappeared and the size of the tumor began to decrease. The origin of these tumors is discussed and the various theories which have been put forward are considered. The method of treatment must vary according to the localization and fixity of the tumor, the age of the patient, and the risk of injuring the reproductive organs.

The Chorionepithelioma of the Male. O. Jüngling. Strahlentherapie, 1937, **60**, 86.

The author observed two cases of chorionepithelioma in the male. One patient was 27 years old, had tuberculosis of the lungs five years before, and had been treated for tuberculous peritonitis. Six months before admission he developed shortness of breath and bloody sputum which led to the diagnosis of tuberculosis. X-ray examination of the lung, however, showed miliary metastases distributed through the entire chest, and careful examination revealed that this was secondary to a tumor of the right testicle which histologically turned out to be a chorionepithelioma. Several treatments with high voltage roentgen rays were without benefit and did not delay the fatal outcome. The second patient was 26 years old and developed pain in the back radiating into the right thigh eight weeks previous to admission. A retroperitoneal tumor which apparently originated from a small tumor in the right testicle was found. Histological examination proved this to be a chorionepithelioma. There were numerous metastases throughout both lungs. The Aschheim-Zondek test in the urine was positive. The tumor in the abdomen was entirely resistant to roentgen rays. The patient died shortly afterward with metastases in the brain. The differential diagnosis between this tumor and the seminoma is discussed.

ERNST A. POHLE, M.D., Ph.D.

The Relative Importance of Histological Analysis in Tumor Therapy. Ferdinand C. Helwig. Am. Jour. Roentgenol. and Rad. Ther., March, 1937, **37**, 358–364.

Histologic analysis provides but a portion of the data necessary for the intelligent treatment of each individ-

ual tumor. It cannot be emphasized too strongly that complete clinical and roentgenographic information is necessary and that individual tumors may vary in response.

S. M. ATKINS, M.D.

Roentgen Therapy of Superficial Tumors. P. Ott. Strahlentherapie, 1937, **59,** 189.

In view of the fact that many technics are used in the treatment of superficial malignancies, the author undertook a systematic study of this problem. Following a brief historical sketch he describes the apparatus used by him in his studies. Four different types of x-ray tubes were available. One could be operated at 10–40 kv., 3 ma., one at 30–75 kv., 3 ma., one at 60 kv., 2 ma., and one at 60–180 kv., 6 ma. The potential was furnished by transformers with valve tubes and condensers. He gives data on the output of the various tubes, depth dose percentages determined in a water phantom, and compares these with the doses obtained from radon screens. The back-scatter for various field sizes was also determined.

It appeared that no routine method can be recommended for the treatment of superficial malignancies, but the method or methods must be selected for each individual patient in order to obtain good results. There is no question but that superficial tumors may react favorably to heavy doses of roentgen rays. However, it is impossible to state at this time whether roentgen rays or radium would produce the best end-results. Eight illustrative case reports are appended to the article with photographs showing the lesions before and after treatment.

ERNST A. POHLE, M.D., Ph.D.

Enormous Tumor of the Breast Treated and Cured by X-rays Filtered through Three Millimeters Aluminum Only. M. T. Nogier. Bull. et Mém. Soc. Radiol. Méd. de France, January, 1937, **25,** 91–93.

In September, 1930, a woman 78 years of age with a breast tumor 14 × 10 × 6 cm., freely movable, and without clinical metastases, but draining pus from three large sinuses, was treated with x-rays by the author. Technic: Coolidge tube, 3 mm. aluminum filter, 30 cm. S.T.D., 25 cm. point spark gap, 1,100 R (Solomon). Three large fields were treated at three-day intervals, and a second series was given after two months. Primary regression of the tumor was remarkable.

In June, 1934, recurrence at the site of one of the fistulas occurred with a small axillary node in evidence. A similar series, dosage 1,900 R, with 8 cm. fields to the breast and two doses of 1,900 R and 800 R to the axillary nodule, were given in September, 1934. The recurrent and axillary nodules disappeared and in November, 1936, the patient, now 84 years of age, was free of recurrence.

S. RICHARD BEATTY, M.D.

Indications for the Treatment of Malignant Tumors of Skin, Mouth, and Larynx. H. Th. Schreus. Strahlentherapie, 1937, **60,** 178.

The indications given by the author are essentially the same as accepted by American radiologists with one principal difference. While in this country it is considered preferable to use radon implantation for many intra-oral tumors, the author uses, whenever possible, the technic developed by Chaoul, namely, roentgen rays applied at a very short focal-skin distance.

ERNST A. POHLE, M.D., Ph.D.

The Experience in Zürich with the Irradiation of Malignant Tumors of the Glandular Organs in the Abdomen Excluding Gonads (1919–1935). H. R. Schinz. Strahlentherapie, 1937, **60,** 170.

This is a résumé of the results obtained in the treatment of malignant tumors of the glandular abdominal organs, published in detail in book form by the author in collaboration with Zuppinger. The many statistics given in the paper cannot be abstracted; suffice it to say, therefore, that a total of 244 cases of this type were seen, of which 146 were males and 98 females; the average age amounted to 51.3 years. At the time of writing the report 12 were still free from symptoms, which corresponds to 5 per cent. After a three-year observation period six, or 2 per cent, died. Palliation was obtained in 85 patients (38 per cent). The average duration of life of all uncured patients was 9.4 months.

ERNST A. POHLE, M.D., Ph.D.

Application of Ultra-short Waves, with Special Regard to Malignant Tumors. W. A. G. van Everdingen. Acta Radiologica, August, 1937, **18,** 559–563.

The influence of ultra-short waves on malignant tissue of mice was studied. The author discusses an objective method for measuring and controlling thermoelectrically the rise of temperature of the test animal during the irradiation. He failed to find any action other than the diathermal one.

G. E. BURCH, M.D.

ULTRA-VIOLET LIGHT

Are Exposures to Ultra-violet and Sun Radiation Dangerous? G. Miescher. Strahlentherapie, 1937, **60,** 134.

The author has studied the changes which occur following continuous exposure to ultra-violet and sun rays in animals, especially with the possibility of producing cancer. He concludes that there is no reason to warn against light and sun exposure if sharp reactions are avoided. Our experience from animal experiments indicates that the face should be protected during general body exposure.

ERNST A. POHLE, M.D., Ph.D.

Sensitization of the Skin to Ultra-violet Light. Fr. Bering. Strahlentherapie, 1937, **60**, 16.

This is a preliminary report as to the effect of certain food, diseases, and chemical agents on the reaction of the human skin to ultra-violet light. The author found, for instance, that in the second and third stages of syphilis the susceptibility is increased, while during the latent period normal reactions were observed. A number of drugs were also tried; prontosil decreased the susceptibility, salvarsan increased it. Experiments studying the effect of others are under way.

ERNST A. POHLE, M.D., Ph.D.

URETHRA (CANCER OF)

Carcinoma of the Female Urethra: Case Report, with Summary and Review of the Literature. T. P. Sparks, Jr., and W. H. Parsons. Urol. and Cutan. Rev., March, 1937, **41**, 157–163. (Reprinted by permission from British Med. Jour., May 1, 1937, page 72 of Epitome of Current Medical Literature.)

The authors have collected 119 cases from the literature as well as a personal one in a patient, 75 years of age, in whom the growth was successfully excised. They state that carcinoma of the female urethra, though uncommon, is not so rare as the number of reported cases would suggest. The ages of the patients ranged from 26 to 75, the average age being 54. Of the group (119), 15 survived three or more years after treatment; 39 received surgical treatment alone, and of these, two lived three years and one five years after operation. Of 40 treated by radium or deep x-ray therapy, six survived three years or more and five were living at the end of five years. Of 21 treated by a combination of some surgical procedure with radium or deep x-ray therapy, seven lived three years or longer and five lived five years or longer after treatment. Of 17 with demonstrable glandular involvement at the time of treatment, six were treated by operation only and one survived three years; seven by radiation alone and none survived as long as three years; three by a combination of operation and radiation, and two survived three years or longer—one nine years. One patient had no treatment.

The prognosis in carcinoma of the female urethra is exceedingly poor, though not hopeless. The authors conclude that desiderata for successful treatment are examination of all patients with painful micturition, early diagnosis of the malignant type, and complete excision in the early stage.

THE UTERUS

Some Considerations in the Treatment of Carcinoma of the Cervix by Irradiation. A. Pickhan. Strahlentherapie, 1937, **60**, 505.

Following a brief discussion of the biologic and physical principles underlying radiation therapy in carcinoma of the cervix, the author outlines the technic as practised in his clinic. In the first two groups roentgen deep therapy is given as a supplementary treatment to radium application. In addition to from 7,000 to 8,000 mg.-hr., a total surface dose of 3,500 r is used. In Groups III and IV roentgen therapy is used almost exclusively except that vaginal radium application is used whenever feasible. A statistical analysis of 1,536 cases seen during the period from 1926 to 1935 showed that 54 per cent of all patients who successfully completed the primary course of treatments were still free from recurrence after 10 years, while the corresponding figure for Group I alone was 69 per cent.

ERNST A. POHLE, M.D., Ph.D.

Has Our Discard of Operative Therapy in Uterine Fibroids and Preclimacteric Metropathies Proved to be Good Practice? C. J. Gauss. Strahlentherapie, 1937, **60**, 401.

The author analyzes in this paper 1,048 cases of uterine fibroids and preclimacteric uterine bleeding, which had been treated by radiation. His indications were to subject only such cases to treatment as had definite symptoms requiring attention. For operation, he considered only a few types of uterine fibroids; as, for instance, submucous, pedunculated, subserous, and infected fibroids. The statistical analysis showed that 93 patients were operated on and the remaining 955 were irradiated. Roentgen rays alone were used in 711 patients, radium alone in 160, and roentgen rays and radium in 16 patients. There was no mortality among those radiated and 4.3 per cent in those operated on. A careful follow-up of the treated cases led the author to the final conclusion that uterine fibroids and preclimacteric metropathies are better irradiated unless there are very definite contra-indications.

ERNST A. POHLE, M.D., Ph.D.

Therapy of Cancer of Uterine Cervix at Gynecologic Clinic in Kiel from Oct. 1, 1922, to Dec. 31, 1930. R. Schröder. Zentralbl. f. Gynäk., March 6, 1937, **61**, 546–563. (Reprinted by permission from British Med. Jour., May 29, 1937, p. 1144 of Epitome of Current Medical Literature.)

The author gives an account of treatment of carcinoma of the cervix and its results in a series of 604 cases (1922–1930) in which a five-year supervision was subsequently possible. "Absolute cure" in the sense of a five-year survival in good health was obtained in 171, or 28 per cent. Increasingly good judgment in selection in the mode of treatment for particular cases, together with increasing experience in all treatments, seemed to bring about an improvement in the results: for the last three years (1928–1930) 327 cases had 34 per cent of five-year cures. For the whole period the operability rate was 58 per cent. The cases actually operated on totalled 50 per cent. Wertheim's operation was usually done in the first and Schauta's vaginal wide hysterectomy in the second half of the period under review. The primary mortality of the 178 Wertheim cases

was 18 per cent, of the 124 Schauta cases 1.5 per cent. The Schauta cases had also a superior percentage of lasting cures—51 per cent, as compared with 36 per cent for the Wertheim cases.

Radium treatment was given in 253 cases, including 51 which were operable: the mean dose was 2,000 mg. radium-element hours in fractional doses. In the operable cases this treatment led to a single death and lasting cures amounting to 42 per cent. In the inoperable cases (202) there was an 8.5 per cent primary mortality and 16.5 per cent of five-year survivals. (The recent radium mortality has been 4 per cent.) Considerable value in prevention of recurrences is ascribed to persistence with post-operative x-radiations in small dosage.